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# UniProtKB/Swiss-Prot entry P57785



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[\[Keywords\]](#) [\[Features\]](#) [\[Sequence\]](#) [\[Tools\]](#)

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## Entry information

Entry name	<b>LEFTB_MOUSE</b>
Primary accession number	<b>P57785</b>
Secondary accession numbers	None
Integrated into Swiss-Prot on	February 21, 2001
Sequence was last modified on	February 21, 2001 (Sequence version 1)
Annotations were last modified on	February 7, 2006 (Entry version 31)
<b>Name and origin of the protein</b>	
Protein name	<b>Left-right determination factor B [Precursor]</b>
Synonym	<b>Lefty-2 protein</b>
Gene name	<b>Name: Leftb</b> Synonyms: Lefty2
From.	Mus musculus (Mouse) [TaxID: 10090]
Taxonomy	Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Euarchontoglires; Glires; Rodentia; Sciurognathi; Muroidea; Muridae; Murinae; Mus

## References

### [1] NUCLEOTIDE SEQUENCE.

PubMed=9348041 [NCBI, ExPASy, EBI, Israel, Japan]  
Meno C., Ito Y., Saijoh Y., Matsuda Y., Tashiro K., Kuhara S., Hamada H.;  
"Two closely-related left-right asymmetrically expressed genes, lefty-1 and lefty-2: their differential expression domains, chromosomal linkage and direct neuralizing activity in Xenopus embryos.";  
Genes Cells 2:513-524(1997).

## Comments

- **FUNCTION:** Morphogen for left-right asymmetry determination of organ systems in mammals.
- **SUBCELLULAR LOCATION:** Secreted protein.

- **DEVELOPMENTAL STAGE:** At the primitive streak stage (E7.0), expressed in the eme mesoderm. By E8.0, expressed exclusively on the left side of developing embryos with expression predominantly in the lateral-plate mesoderm (LPM). Weak expression in the prospective floor plate (PFP).
- **PTM:** The processing of the protein may also occur at the second R-X-X-R site located 132-135. Processing appears to be regulated in a cell-type specific manner.
- **SIMILARITY:** Belongs to the TGF-beta family.

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### Cross-references

#### 3D structure databases

HSSP P10600; 1TGJ. [HSSP ENTRY / PDB]  
ModBase P57785.

#### Protein-protein interaction databases

DIP P57785.

#### 2D gel databases

SWISS-2DPAGE Get region on 2D PAGE.

#### Organism-specific gene databases

MGI MGI:1277956; Leftb.  
GeneLynx Leftb; Mus musculus.  
HOVERGEN [Family / Alignment / Tree]

#### Gene expression databases

CleanEx MGI:1277956; Leftb.

#### Family and domain databases

InterPro IPR001839; TGFb.  
IPR003942; TGFb4.  
IPR001111; TGFb\_N.  
Graphical view of domain structure.  
Pfam PF00019; TGF\_beta; 1.  
PF00688; TGFb\_propeptide; 1.  
Pfam graphical view of domain structure.  
PRINTS PR01427; TGFBETA4.  
ProDom PD000357; TGFb; 1.  
[Domain structure / List of seq. sharing at least 1 domain]  
SMART SM00204; TGFB; 1.  
SMART graphical view of domain structure.  
PROSITE PS00250; TGF\_BETA\_1; 1.  
BLOCKS P57785.

#### Genome annotation databases

Ensembl ENSMUSG00000038793; Mus musculus. [Contig view]

#### Other

SOURCE Leftb; Mus musculus.

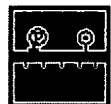
ProtoNet P57785.

UniRef View cluster of proteins with at least 50% / 90% / 100% identity.

### Keywords

**Cytokine; Developmental protein; Glycoprotein; Growth factor; Signal.**

### Features



Feature table viewer



Feature aligner

Key	From	To	Length	Description	FTId
SIGNAL	1	21	21	By similarity.	
PROPEP	22	77	56	Or 135 (Potential).	PRO_0000033812
CHAIN	78	368	291	Left-right determination factor B.	PRO_0000033813
CARBOHYD	158	158		N-linked (GlcNAc...) (Potential).	
DISULFID	253	266		By similarity.	
DISULFID	265	318		By similarity.	
DISULFID	295	353		By similarity.	
DISULFID	299	355		By similarity.	

### Sequence information

Length: **368 AA** [This is the length of the unprocessed precursor]

Molecular weight: **41141 Da** [This is the MW of the unprocessed precursor]

CRC64: **56B5ED095167A6C3**  
is a checksum on the sequence

<u>10</u>	<u>20</u>	<u>30</u>	<u>40</u>	<u>50</u>	<u>60</u>
MKSLWLCWAL	WVLPLAGPGA	AMTEEQVLSS	LLQQLQLSQA	PTLDSADVEE	MAIPTHVRSQ
<u>70</u>	<u>80</u>	<u>90</u>	<u>100</u>	<u>110</u>	<u>120</u>
YVALLQGSHA	DRSRGKRFSQ	NLREVAGRFL	MSETSTHLLV	FGMEQRLPPN	SELVQAVLRL
<u>130</u>	<u>140</u>	<u>150</u>	<u>160</u>	<u>170</u>	<u>180</u>
FQEPVVRTAL	RRFERLSPHS	ARARVTIEWL	RVREDGSNRT	ALIDSRLVSI	HESGWKAFDV
<u>190</u>	<u>200</u>	<u>210</u>	<u>220</u>	<u>230</u>	<u>240</u>
TEAVNFWQQL	SRPRQPLLLQ	VSVQREHLGP	GTWSAHKLVR	FAAQGTPDGK	GQGEPQLELH
<u>250</u>	<u>260</u>	<u>270</u>	<u>280</u>	<u>290</u>	<u>300</u>
TLDLKDYGAA	GNCDEVPVPT	EGTRCCRQEM	YLDLQGMKWA	ENWILEPPGF	LTYESCVGSL
<u>310</u>	<u>320</u>	<u>330</u>	<u>340</u>	<u>350</u>	<u>360</u>
QLPESLTIGW	PFLGPRQCVA	SEMTSLPMIV	SVKEGGTRTP	QVVSLPNMRV	QTCSCASDGA
LIPRGIDL					

Pf  
in  
F/  
foi

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*View entry in raw text format (no links)*

*Report form for errors/updates in this UniProtKB/Swiss-Prot entry*

**BLAST**

BLAST submission on  
ExPASy/SIB  
or at NCBI (USA)



Sequence analysis tools: ProtParam,  
ProtScale, Compute pI/Mw, PeptideMass,  
PeptideCutter, Dotlet (Java)



ScanProsite, MotifScan



Submit a homology modeling request to  
SWISS-MODEL



NPSA Sequence  
analysis tools



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If results of this search are reported or published, please mention that the computation was performed at the SIB using the BLAST network service. The SIB BLAST network service uses a server developed at SIB and the BLAST 2 software.

In case of problems, please read the online BLAST help.  
If your question is not covered, please contact <helpdesk@expasy.org>

NCBI BLAST program reference [PMID:9254694]:  
Altschul S.F., Madden T.L., Schäffer A.A., Zhang J., Zhang Z., Miller W., Lipman D.J. Gapped BLAST and PSI-BLAST: a new generation of protein database search programs. Nucleic Acids Res. 25:3389-3402(1997).

=====

Query: 16 AA

Date run: 2006-06-23 17:03:24 UTC+0100 on blast01.vital-it.ch

Program: NCBI BLASTP 2.2.13 [Nov-27-2005]

Database: UniProtKB

3,203,912 sequences; 1,050,329,766 total letters

UniProt Knowledgebase Release 8.1 consists of:

UniProtKB/Swiss-Prot Release 50.1 of 13-Jun-2006: 223100 entries

UniProtKB/TrEMBL Release 33.1 of 13-Jun-2006: 2965756 entries

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### List of potentially matching sequences

Send selected sequences to

☐ Include query sequence

Db	AC	Description
----	----	-------------

<input type="checkbox"/>	sp O00292	TGFB4_HUMAN Transforming growth factor beta-4 precursor.
--------------------------	-----------	--

<input type="checkbox"/>	sp O75610	LEFTB_HUMAN Left-right determination factor B precursor.
--------------------------	-----------	--

- ☐ tr Q5TE89 \_HUMAN Left-right determination factor 2 [LEFTY2] [Homo
- ☐ tr Q5TE94 \_HUMAN Left-right determination factor 1 [LEFTY1] [Homo
- ☐ tr Q53H67 \_HUMAN Left-right determination, factor B preproprotein
- ☐ sp Q64280 TGFB4\_MOUSE Transforming growth factor beta-4 precursor.
- ☐ tr Q3V2A9 \_MOUSE ES cells cDNA, RIKEN full-length enriched librar
- ☐ sp P57785 LEFTB\_MOUSE Left-right determination factor B precursor.
- ☐ tr Q52M97 \_XENLA Hypothetical protein [Xenopus laevis (African cl
- ☐ tr Q8BMF7 \_MOUSE 13 days embryo male testis cDNA, RIKEN full-leng
- ☐ tr Q5UCE3 \_RAT EBAF precursor [Rattus norvegicus (Rat)]
- ☐ tr Q213F2 \_RHOPB Alpha/beta hydrolase fold [RPC\_2939] [Rhodopseud

### Graphical overview of the alignments

[Click here](#)

to resubmit your query after masking regions matching PROSITE profiles or Pfam HMMs

(?) Help) (use ScanProsite for more details about PROSITE matches)

#### Profile hits

#### Pfam hits

#### Matches on query sequence

#### Submission

TGFB4\_HUMAN  
LEFTB\_HUMAN  
Q5TE89\_HUMAN  
Q5TE94\_HUMAN  
Q53H67\_HUMAN  
TGFB4\_MOUSE  
Q3V2A9\_MOUSE  
LEFTB\_MOUSE  
Q52M97\_XENLA  
Q8BMF7\_MOUSE  
Q5UCE3\_RAT  
Q213F2\_RHOPB

#### Submission

Identity 0 25 50 75 100%

### Alignments

sp 000292 Transforming growth factor beta-4 precursor (TGF-beta-4) 366 AA  
TGFB4\_HUMAN (Endometrial bleeding-associated factor) (Left-right  
determination factor A) (Lefty-A protein) [EBAF] [Homo sapiens (Human)] align

Score = 43.5 bits (95), Expect = 8e-04

Identities = 13/13 (100%), Positives = 13/13 (100%)

Query: 1 CASDGALVPRRLQ 13  
CASDGALVPRRLQ  
Sbjct: 353 CASDGALVPRRLQ 365

sp O75610 Left-right determination factor B precursor (Lefty-B 366  
LEFTB\_HUMAN protein) AA  
[LEFTB] [Homo sapiens (Human)] align

Score = 43.5 bits (95), Expect = 8e-04  
Identities = 13/13 (100%), Positives = 13/13 (100%)

Query: 1 CASDGALVPRRLQ 13  
CASDGALVPRRLQ  
Sbjct: 353 CASDGALVPRRLQ 365

tr Q5TE89 Left-right determination factor 2 [LEFTY2] [Homo sapiens 366  
Q5TE89\_HUMAN (Human)] AA  
align

Score = 43.5 bits (95), Expect = 8e-04  
Identities = 13/13 (100%), Positives = 13/13 (100%)

Query: 1 CASDGALVPRRLQ 13  
CASDGALVPRRLQ  
Sbjct: 353 CASDGALVPRRLQ 365

tr Q5TE94 Left-right determination factor 1 [LEFTY1] [Homo sapiens 366  
Q5TE94\_HUMAN (Human)] AA  
align

Score = 43.5 bits (95), Expect = 8e-04  
Identities = 13/13 (100%), Positives = 13/13 (100%)

Query: 1 CASDGALVPRRLQ 13  
CASDGALVPRRLQ  
Sbjct: 353 CASDGALVPRRLQ 365

tr Q53H67 Left-right determination, factor B preproprotein variant 366  
Q53H67\_HUMAN (Fragment) AA  
[LEFTY1] [Homo sapiens (Human)] align

Score = 43.5 bits (95), Expect = 8e-04  
Identities = 13/13 (100%), Positives = 13/13 (100%)

Query: 1 CASDGALVPRRLQ 13  
CASDGALVPRRLQ  
Sbjct: 353 CASDGALVPRRLQ 365

sp Q64280 Transforming growth factor beta-4 precursor (TGF-beta-4) 368  
TGFB4\_MOUSE (Lefty AA  
protein) (Lefty-1 protein) (STRA3 protein) [Ebf] [Mus align  
musculus (Mouse)]

Score = 41.4 bits (90), Expect = 0.004  
Identities = 12/13 (92%), Positives = 13/13 (100%)

Query: 1 CASDGALVPRRLQ 13  
CASDGAL+PRRLQ  
Sbjct: 355 CASDGALIPRRLQ 367

tr Q3V2A9 ES cells cDNA, RIKEN full-length enriched library, 368  
Q3V2A9\_MOUSE clone:2410018B15 AA  
product:left-right determination, factor B, full insert align  
sequence [Lefty1] [Mus musculus (Mouse)]

Score = 41.4 bits (90), Expect = 0.004  
Identities = 12/13 (92%), Positives = 13/13 (100%)

Query: 1 CASDGALVPRRLQ 13  
CASDGAL+PRRLQ  
Sbjct: 355 CASDGALIPRRLQ 367

sp P57785 Left-right determination factor B precursor (Lefty-2) 368  
LEFTB\_MOUSE protein) AA  
[Leftb] [Mus musculus (Mouse)] align

Score = 31.6 bits (67), Expect = 3.2  
Identities = 9/10 (90%), Positives = 10/10 (100%)

Query: 1 CASDGALVPR 10  
CASDGAL+PR  
Sbjct: 355 CASDGALIPR 364

tr Q52M97            **Hypothetical protein [Xenopus laevis (African clawed**            368  
Q52M97\_XENLA **frog)]**            AA  
align

Score = 31.6 bits (67), Expect = 3.2  
Identities = 9/10 (90%), Positives = 10/10 (100%)

Query: 1    CASDGALVPR 10  
          CASDGAL+PR  
Sbjct: 355 CASDGALIPR 364

tr Q8BMF7            **13 days embryo male testis cDNA, RIKEN full-length**            368  
Q8BMF7\_MOUSE **enriched**            AA  
          **library, clone:6030463A22 product:LEFT-RIGHT**  
          **DETERMINATION FACTOR B (LEFTY-2 PROTEIN), full insert**  
          **sequence (Left-right determination factor 2) [Lefty2]**  
          **[Mus musculus (Mouse)]**            align

Score = 31.6 bits (67), Expect = 3.2  
Identities = 9/10 (90%), Positives = 10/10 (100%)

Query: 1    CASDGALVPR 10  
          CASDGAL+PR  
Sbjct: 355 CASDGALIPR 364

tr Q5UCE3            **EBAF precursor [Rattus norvegicus (Rat)]** 366 AA  
Q5UCE3\_RAT  
align

Score = 31.6 bits (67), Expect = 3.2  
Identities = 9/10 (90%), Positives = 10/10 (100%)

Query: 1    CASDGALVPR 10  
          CASDGAL+PR  
Sbjct: 353 CASDGALIPR 362

tr Q213F2            **Alpha/beta hydrolase fold [RPC\_2939] [Rhodopseudomonas**            348  
Q213F2\_RHOPB **palustris**            AA  
          **(strain BisB18)]**            align

Score = 30.8 bits (65), Expect = 5.7  
Identities = 8/9 (88%), Positives = 9/9 (100%)

Query: 8 VPRRLQHRP 16  
VPRR+QHRP  
Sbjct: 3 VPRRMQHRP 11

Database: UniProtKB

Posted date: Jun 13, 2006 4:15 PM  
Number of letters in database: 996,946,033  
Number of sequences in database: 3,053,606

Database: /home/local/blastnet/database/EXPASY//UniProtKB.01

Posted date: Jun 13, 2006 4:16 PM  
Number of letters in database: 53,383,733  
Number of sequences in database: 150,306

Lambda	K	H
0.351	0.293	1.84

Gapped

Lambda	K	H
0.294	0.110	0.610

Matrix: PAM30

Gap Penalties: Existence: 9, Extension: 1  
Number of Hits to DB: 6,395,476  
Number of Sequences: 3203912  
Number of extensions: 10474  
Number of successful extensions: 1557  
Number of sequences better than 10.0: 12  
Number of HSP's better than 10.0 without gapping: 12  
Number of HSP's successfully gapped in prelim test: 0  
Number of HSP's that attempted gapping in prelim test: 1545  
Number of HSP's gapped (non-prelim): 12  
length of query: 16  
length of database: 1,050,329,766  
effective HSP length: 6  
effective length of query: 10  
effective length of database: 1,031,106,294  
effective search space: 10311062940  
effective search space used: 10311062940  
T: 16  
A: 15  
X1: 14 ( 7.1 bits)  
X2: 35 (14.8 bits)  
X3: 58 (24.6 bits)

S1: 40 (22.0 bits)

S2: 64 (30.3 bits)

Wallclock time: 3 seconds



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# UniProtKB/Swiss-Prot entry Q64280



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[\[Keywords\]](#) [\[Features\]](#) [\[Sequence\]](#) [\[Tools\]](#)

*Note: most headings are clickable, even if they don't appear as links. They link to the user manual or other documents.*

## Entry information

Entry name	<b>TGFB4_MOUSE</b>
Primary accession number	<b>Q64280</b>
Secondary accession numbers	None
Integrated into Swiss-Prot on	November 1, 1997
Sequence was last modified on	November 1, 1996 (Sequence version 1)
Annotations were last modified on	April 18, 2006 (Entry version 47)

## Name and origin of the protein

Protein name	<b>Transforming growth factor beta-4 [Precursor]</b>
Synonyms	<b>TGF-beta-4</b> <b>Lefty protein</b> <b>Lefty-1 protein</b> <b>STRA3 protein</b>
Gene name	<b>Name: Ebaf</b>
From	Synonyms: Lefty, Lefty1, Stra3, Tgfb4
Taxonomy	Mus musculus (Mouse) [TaxID: 10090] Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Euarchontoglires; Glires; Rodentia; Sciurognathi; Muroidea; Muridae; Murinae; Mus

## References

### [1] NUCLEOTIDE SEQUENCE.

DOI=10.1038/381151a0; PubMed=8610011 [NCBI, ExPASy, EBI, Israel, Japan]  
Meno C., Saijoh Y., Fujii H., Ikeda M., Yokoyama T., Yokoyama M., Toyoda Y., Hamada T.  
"Left-right asymmetric expression of the TGF beta-family member lefty in mouse embryos  
Nature 381:151-155(1996).

### [2] NUCLEOTIDE SEQUENCE.

Bouillet P.;  
Submitted (JUN-1996) to the EMBL/GenBank/DDBJ databases.



**[3] NUCLEOTIDE SEQUENCE.**

PubMed=9496783 [NCBI, ExPASy, EBI, Israel, Japan]

Oulad-Abdelghani M., Chazaud C., Bouillet P., Mattei M.-G., Dolle P., Chambon P.;

"Stra3/lefty, a retinoic acid-inducible novel member of the transforming growth factor-beta superfamily.";

Int. J. Dev. Biol. 42:23-32(1998).

**[4] NUCLEOTIDE SEQUENCE [LARGE SCALE MRNA].****TISSUE**=Embryonic stem cell;

DOI=10.1073/pnas.242603899; PubMed=12477932 [NCBI, ExPASy, EBI, Israel, Japan]

Strausberg R.L., Feingold E.A., Grouse L.H., Derge J.G., Klausner R.D., Collins F.S., Wang L., Shenmen C.M., Schuler G.D., Altschul S.F., Zeeberg B., Buetow K.H., Schaefer C.F., L.N.K., Hopkins R.F., Jordan H., Moore T., Max S.I., Wang J., Marra M.A.;

"Generation and initial analysis of more than 15,000 full-length human and mouse cDNA sequences.";

Proc. Natl. Acad. Sci. U.S.A. 99:16899-16903(2002).

**[5] FUNCTION.**DOI=10.1016/S0092-8674(00)81472-5; PubMed=9708731 [NCBI, ExPASy, EBI, Israel, Japan]  
Meno C., Shimono A., Saijoh Y., Yashiro K., Mochida K., Ohishi S., Noji S., Kondoh H., Hamada H.;

"Lefty-1 is required for left-right determination as a regulator of lefty-2 and nodal.";

Cell 94:287-297(1998).

**Comments**

- **FUNCTION:** Required for left-right axis determination as a regulator of LEFTY2 and NO
- **SUBCELLULAR LOCATION:** Secreted protein.
- **DEVELOPMENTAL STAGE:** By E8.0, expressed exclusively on the left side of develop embryos with expression predominantly in the prospective floor plate (PFP). Weak expression in the lateral-plate mesoderm (LPM).
- **PTM:** The processing of the protein may also occur at the second R-X-X-R site located 132-135. Processing appears to be regulated in a cell-type specific manner.
- **SIMILARITY:** Belongs to the TGF-beta family.

**Copyright**Copyrighted by the UniProt Consortium, see <http://www.uniprot.org/terms>. Distributed under the Creative Commons Attribution-NoDerivs License.**Cross-references****Sequence databases**

EMBL	D83921; BAA12121.1; -; mRNA.	[EMBL / GenBank / DDBJ] [CoDingSequence]
	Z73151; CAA97497.1; -; mRNA.	[EMBL / GenBank / DDBJ] [CoDingSequence]
	AJ000082; CAA03909.1; -; mRNA.	[EMBL / GenBank / DDBJ] [CoDingSequence]
	AJ000083; CAA03910.1; -; Genomic_DNA.	[EMBL / GenBank / DDBJ] [CoDingSequence]
	BC050221; AAH50221.1; -; mRNA.	[EMBL / GenBank / DDBJ] [CoDingSequence]
PIR	S67507; S67507.	
UniGene	Mm.378911	

### 3D structure databases

HSSP P10600; 1TGJ. [HSSP ENTRY / PDB]

ModBase Q64280.

### Protein-protein interaction databases

DIP Q64280.

### 2D gel databases

SWISS-2DPAGE Get region on 2D PAGE.

### Organism-specific gene databases

MGI MGI:107405; Ebaf.

GeneLynx Ebaf; Mus musculus.

HOVERGEN [Family / Alignment / Tree]

### Gene expression databases

CleanEx MGI:107405; Ebaf.

### Ontologies

GO GO:0009948; Biological process: anterior/posterior axis specification (*inferred from genetic interaction*).  
 GO GO:0042074; Biological process: cell migration during gastrulation (*inferred from genetic interaction*).  
 GO GO:0008285; Biological process: negative regulation of cell proliferation (*inferred from genetic interaction*).  
 QuickGo view.

### Family and domain databases

InterPro IPR001839; TGFb.  
 IPR003942; TGFb4.  
 IPR001111; TGFb\_N.  
 Graphical view of domain structure.  
 Pfam PF00019; TGF\_beta; 1.  
 PF00688; TGFb\_propeptide; 1.  
 Pfam graphical view of domain structure.  
 PRINTS PR01427; TGFBETA4.  
 ProDom PD000357; TGFb; 1.  
 [Domain structure / List of seq. sharing at least 1 domain]  
 SMART SM00204; TGFB; 1.  
 SMART graphical view of domain structure.  
 PROSITE PS00250; TGF\_BETA\_1; 1.  
 BLOCKS Q64280.

### Genome annotation databases

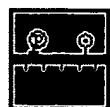
Ensembl ENSMUSG00000038793; Mus musculus. [Contig view]

### Other

SOURCE Ebaf; Mus musculus.

ProtoNet Q64280.

UniRef View cluster of proteins with at least 50% / 90% / 100% identity.

**Keywords****Cytokine; Developmental protein; Glycoprotein; Growth factor; Signal.****Features**

Feature table viewer



Feature aligner

Key	From	To	Length	Description	FTId
SIGNAL	1	21	21	Potential.	
PROPEP	22	76	55	Or 135 (Potential).	PRO_0000033808
CHAIN	77	368	292	Transforming growth factor beta-4.	PRO_0000033809
CARBOHYD	158	158		N-linked (GlcNAc...) (Potential).	
DISULFID	253	266		By similarity.	
DISULFID	265	318		By similarity.	
DISULFID	295	353		By similarity.	
DISULFID	299	355		By similarity.	

**Sequence information**Length: **368 AA** [This is the length of the unprocessed precursor]Molecular weight: **41498 Da** [This is the MW of the unprocessed precursor]CRC64: **821DAE663C546B5F**  
is a checksum on the sequence

```

      10      20      30      40      50      60
MPFLWLCWAL WALSLVSLRE ALTGEQILGS LLQQQLQLDQP PVLDKADVEG MVIPSHVRTQ

      70      80      90     100     110     120
YVALLQHSHA SRSRGKRFSQ NLREVAGRFL VSETSTHLLV FGMEQRLPPN SELVQAVLRL

     130     140     150     160     170     180
FQEPVPRTAL RRQKRLSPHS ARARVTIEWL RFRDDGSNRT ALIDSRLVSI HESGWKAFDV

     190     200     210     220     230     240
TEAVNFWQQ L SRPRQPLLLQ VSVQREHLGP GTWSSHKLV R FAAQGTPDGK GQGEPQLELH

     250     260     270     280     290     300
TLDLKDYGAQ GNCDPEAPVT EGTRCCRQEM YLDLQGMKWA ENWILEPPGF LTYECVGSCL

     310     320     330     340     350     360
QLPESLTSRW PFLGPRQCVA SEMTSLPMIV SVKEGGRT RP QVVSLPNMRV QTCSCASDGA

LIPRRLQP

```

Q64280  
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## . CLUSTAL W (1.81) multiple sequence alignment

```

unk|VIRT1035|Blast_submission -----
sp|Q64280|TGFB4_MOUSE      MPFLWLCWALWALSLSLREALTGEQILGSLLQQLQLDQPPVLDKADVE

unk|VIRT1035|Blast_submission -----
sp|Q64280|TGFB4_MOUSE      MVIPSHVRTQYVALLQHSHASRSRGKRFSQNLREVAGRFLVSETSTHLL

unk|VIRT1035|Blast_submission -----
sp|Q64280|TGFB4_MOUSE      FGMEQRLPPNSELVQAVLRLFQEPVVRTALRRQRLSPHSARARVTIEW

unk|VIRT1035|Blast_submission -----
sp|Q64280|TGFB4_MOUSE      RFRDDGSNRTALIDSRLVSIHESGWKAFDVTEAVNFWQQLSRPRQPLLL

unk|VIRT1035|Blast_submission -----
sp|Q64280|TGFB4_MOUSE      VSVQREHLGPGTWSSHKLVRFAAQGTPDGKGQGEPOLELHTLDLKDYGA

unk|VIRT1035|Blast_submission -----
sp|Q64280|TGFB4_MOUSE      GNCDPEAPVTEGTRCCRQEMYLDLQGMKWAENWILEPPGFLTYECVGSC

unk|VIRT1035|Blast_submission -----
sp|Q64280|TGFB4_MOUSE      QLPESLTSRWPFGLPRQCVASEMTSLPMIVSVKEGGRTRPQVVSLPNMR

unk|VIRT1035|Blast_submission -----CASDGALVPRRLQHRP
sp|Q64280|TGFB4_MOUSE      QTCSCASDGALIPRRLQ--P
                        *****.*****  *

```

tr	Q3V2A9	ES cells cDNA, RIKEN full-length enriched library,	368
	Q3V2A9_MOUSE	clone:2410018B15	AA
		product:left-right determination, factor B, full insert	align
		sequence [Lefty1] [Mus musculus (Mouse)]	

Score = 41.4 bits (90), Expect = 0.004

Identities = 12/13 (92%), Positives = 13/13 (100%)

Query: 1 CASDGALVPRRLQ 13

CASDGAL+PRRLQ

Sbjct: 355 CASDGALIPRRLQ 367

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# UniProtKB/Swiss-Prot entry O00292



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*Note: most headings are clickable, even if they don't appear as links. They link to the user manual or other documents.*

## Entry information

Entry name	<b>TGFB4_HUMAN</b>
Primary accession number	<b>O00292</b>
Secondary accession numbers	O75611 Q8NBQ9
Integrated into Swiss-Prot on	November 1, 1997
Sequence was last modified on	February 21, 2001 (Sequence version 2)
Annotations were last modified on	June 13, 2006 (Entry version 63)

## Name and origin of the protein

Protein name	<b>Transforming growth factor beta-4 [Precursor]</b>
Synonyms	<b>TGF-beta-4</b> <b>Endometrial bleeding-associated factor</b> <b>Left-right determination factor A</b> <b>Lefty-A protein</b>

Gene name	<b>Name: EBAF</b> Synonyms: LEFTA, LEFTYA, TGFB4 ORFNames: PSEC0024
-----------	---

From	Homo sapiens (Human) [TaxID: 9606]
Taxonomy	Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Euarchontoglires; Primates; Haplorrhini; Catarrhini; Hominidae; Homo.

## References

[1] NUCLEOTIDE SEQUENCE [MRNA].

**TISSUE**=Placenta;

PubMed=9153275 [NCBI, ExPASy, EBI, Israel, Japan]

Kothapalli R., Buyuksal I., Wu S.-Q., Chegini N., Tabibzadeh S.;

"Detection of ebaf, a novel human gene of the transforming growth factor beta superfamily association of gene expression with endometrial bleeding.";

J. Clin. Invest. 99:2342-2350(1997).

[2] NUCLEOTIDE SEQUENCE [GENOMIC DNA], AND VARIANT L-R AXIS MALFORMATIO  
ASN-342.

**TISSUE**=Placenta;

DOI=10.1086/302289; PubMed=10053005 [NCBI, ExPASy, EBI, Israel, Japan]

Kosaki K., Bassi M.T., Kosaki R., Lewin M., Belmont J., Schauer G., Casey B.;

"Characterization and mutation analysis of human LEFTY A and LEFTY B, homologues o  
murine genes implicated in left-right axis development.";

Am. J. Hum. Genet. 64:712-721(1999).

[3] NUCLEOTIDE SEQUENCE [LARGE SCALE MRNA].

**TISSUE**=Teratocarcinoma;

Ota T., Nishikawa T., Suzuki Y., Kawai-Hio Y., Hayashi K., Ishii S., Saito K., Yamamoto J.

Wakamatsu A., Nagai T., Nakamura Y., Nagahari K., Sugano S., Isogai T.;

"HRI human cDNA sequencing project.";

Submitted (MAR-2002) to the EMBL/GenBank/DDBJ databases.

[4] NUCLEOTIDE SEQUENCE [LARGE SCALE MRNA].

**TISSUE**=Ovary;

DOI=10.1073/pnas.242603899; PubMed=12477932 [NCBI, ExPASy, EBI, Israel, Japan]

Strausberg R.L., Feingold E.A., Grouse L.H., Derge J.G., Klausner R.D., Collins F.S., Wa

L., Shenmen C.M., Schuler G.D., Altschul S.F., Zeeberg B., Buetow K.H., Schaefer C.F., I

N.K., Hopkins R.F., Jordan H., Moore T., Max S.I., Wang J., , Marra M.A.;

"Generation and initial analysis of more than 15,000 full-length human and mouse cDNA  
sequences.";

Proc. Natl. Acad. Sci. U.S.A. 99:16899-16903(2002).

**Comments**

- **FUNCTION:** Required for left-right (L-R) asymmetry determination of organ systems in mammals. May play a role in endometrial bleeding.
- **SUBCELLULAR LOCATION:** Secreted protein.
- **TISSUE SPECIFICITY:** Mesenchymal cells of the endometrial stroma.
- **DEVELOPMENTAL STAGE:** Transiently expressed before and during menstrual bleed
- **PTM:** The processing of the protein may also occur at the second R-X-X-R site located 132-135. Processing appears to be regulated in a cell-type specific manner.
- **DISEASE:** Defects in EBAF are the cause of left-right axis malformations (L-R axis malformation) [MIM:601877]. The defect includes left pulmonary isomerism, with cardia anomalies characterized by complete atrioventricular canal defect and hypoplastic left ventricle, and interrupted inferior vena cava.
- **SIMILARITY:** Belongs to the TGF-beta family.
- **CAUTION:** Ref.1 authors have revised their sequence to agree with the one shown in th entry, but have not submitted the revised DNA sequence.
- **WEB RESOURCE:** NAME=GeneReviews; URL="http://www.genetests.org/query?gene=EBAF".

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Attribution-NoDerivs License.

**Cross-references**

**Sequence databases**

U81523; AAB53269.1; ALT\_SEQ; mRNA. [EMBL / GenBank / DDBJ]  
[CoDingSequence]



	AF081511; AAC32600.1; -; Genomic_DNA.	[EMBL / GenBank / DDBJ] [CoDingSequence]
	AF081508; AAC32600.1; JOINED; Genomic_DNA.	[EMBL / GenBank / DDBJ] [CoDingSequence]
	AF081509; AAC32600.1; JOINED; Genomic_DNA.	[EMBL / GenBank / DDBJ] [CoDingSequence]
EMBL	AF081510; AAC32600.1; JOINED; Genomic_DNA.	[EMBL / GenBank / DDBJ] [CoDingSequence]
	AF081513; AAD48145.1; -; mRNA.	[EMBL / GenBank / DDBJ] [CoDingSequence]
	AK075344; BAC11556.1; -; mRNA.	[EMBL / GenBank / DDBJ] [CoDingSequence]
	BC035718; AAH35718.1; -; mRNA.	[EMBL / GenBank / DDBJ] [CoDingSequence]

UniGene Hs.520187

### 3D structure databases

HSSP P10600; 1TGJ. [HSSP ENTRY / PDB]

ModBase O00292.

### Protein-protein interaction databases

DIP O00292.

### Enzyme and pathway databases

Reactome O00292; -.

### 2D gel databases

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### Organism-specific gene databases

H-InvDB HIX0001640; -.

HGNC HGNC:3122; EBAF.

GeneCards EBAF.

GeneLynx EBAF; Homo sapiens.

GenAtlas EBAF.

MIM 601877; gene+phenotype. [NCBI / EBI]

HOVERGEN [Family / Alignment / Tree]

### Gene expression databases

CleanEx HGNC:3122; EBAF.

### Ontologies

GO:0007275; Biological process: development (*traceable author statement*).

GO:0007309; Biological process: oocyte axis determination (*traceable author statement*).

GO GO:0007179; Biological process: transforming growth factor beta receptor sign.  
pathway (*traceable author statement*).

QuickGo  
view.

### Family and domain databases

InterPro IPR001839; TGFb.  
 IPR003942; TGFb4.  
 IPR001111; TGFb\_N.  
 Graphical view of domain structure.  
 Pfam PF00019; TGF\_beta; 1.  
 PF00688; TGFb\_propeptide; 1.  
 Pfam graphical view of domain structure.  
 PRINTS PR01427; TGFBETA4.  
 ProDom PD000357; TGFb; 1.  
 [Domain structure / List of seq. sharing at least 1 domain]  
 SMART SM00204; TGFB; 1.  
 SMART graphical view of domain structure.  
 PROSITE PS00250; TGF\_BETA\_1; 1.  
 BLOCKS O00292.

### Genome annotation databases

Ensembl ENSG00000143768; Homo sapiens. [Contig view]

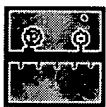
### Other

LinkHub O00292; -.  
 IOH11728; -.  
 RZPD- IOH11866; -.  
 ProtExp T1122; -.  
 W0279; -.  
 SOURCE EBAF; Homo sapiens.  
 ProtoNet O00292.  
 UniRef View cluster of proteins with at least 50% / 90% / 100% identity.

### Keywords

**Cytokine; Developmental protein; Disease mutation; Glycoprotein; Growth factor; Polymorphism; Signal.**

### Features



Feature table viewer



Feature aligner

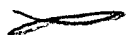
Key	From	To	Length	Description	FTId
SIGNAL	1	21	21	<i>Potential.</i>	
PROPEP	22	76	55	Or 135 ( <i>Potential</i> ).	PRO_000003
CHAIN	77	366	290	Transforming growth factor beta-4.	PRO_000003
CARBOHYD	158	158		N-linked (GlcNAc...) ( <i>Potential</i> ).	
DISULFID	251	264		<i>By similarity.</i>	
DISULFID	263	316		<i>By similarity.</i>	
DISULFID	293	351		<i>By similarity.</i>	
DISULFID	297	353		<i>By similarity.</i>	
VARIANT	92	92	1	S -> L (in dbSNP:366439) [NCBI/Ensembl].	VAR_02198C
VARIANT	286	286	1	P -> L (in dbSNP:2295418) [NCBI/Ensembl].	VAR_021981
VARIANT	342	342	1	S -> N (in L-R axis malformations).	VAR_010385

CONFLICT 183 183 A -&gt; P (in Ref. 3).

**Sequence information**Length: **366 AA** [This is the length of the unprocessed precursor]Molecular weight: **40920 Da** [This is the MW of the unprocessed precursor]CRC64: **63A416CAE30F7A39** is a checksum on the sequence

<u>10</u>	<u>20</u>	<u>30</u>	<u>40</u>	<u>50</u>	<u>60</u>
MWPLWLCWAL	WVLPLAGPGA	ALTEEQLLGS	LLRQLQLSEV	PVLDRADMEK	LVIPAHVRAQ
<u>70</u>	<u>80</u>	<u>90</u>	<u>100</u>	<u>110</u>	<u>120</u>
YVLLRRSHG	DRSRGKRFSQ	SFREVAGRFL	ASEASTHLLV	FGMEQRLPPN	SELVQAVLRL
<u>130</u>	<u>140</u>	<u>150</u>	<u>160</u>	<u>170</u>	<u>180</u>
FQEPVPKAAL	HRHGRLSPRS	AQARVTVEWL	RVRDDGSNRT	SLIDSRLVSV	HESGWKAFDV
<u>190</u>	<u>200</u>	<u>210</u>	<u>220</u>	<u>230</u>	<u>240</u>
TEAVNFWQQL	SRPRQPLLLQ	VSVQREHLGP	LASGAHKLVR	FASQGAPAGL	GEPQLELHTL
<u>250</u>	<u>260</u>	<u>270</u>	<u>280</u>	<u>290</u>	<u>300</u>
DLRDYGAQGD	CDPEAPMTEG	TRCCRQEMYI	DLQGMKWAKN	WVLEPPGFLLA	YECVGTCQQP
<u>310</u>	<u>320</u>	<u>330</u>	<u>340</u>	<u>350</u>	<u>360</u>
PEALAFNWP	LGPRQCIASE	TASLPMIVSI	KEGGRTRPQV	VSLPNMRVQK	CSCASDGALV

PRRLQP

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ProtScale, Compute pI/Mw, PeptideMass,  
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<input type="checkbox"/>	L1	Left-right or Lefty-A	4270
<input type="checkbox"/>	L2	L1 and (cdna or c-dna or gene or genetically or genetic or genes or mrna or clone or plasmid or coding or orf or seq or nucleic or nucleotide or polynucleotide or poly-nucleic or poly-nucleotide or nuclear or chromosomal or chromosome)	435
<input type="checkbox"/>	L3	L1 same (cdna or c-dna or gene or genetically or genetic or genes or mrna or clone or plasmid or coding or orf or seq or nucleic or nucleotide or polynucleotide or poly-nucleic or poly-nucleotide or nuclear or chromosomal or chromosome)	48
		<i>DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD; PLUR=YES; OP=OR</i>	
<input type="checkbox"/>	L4	Left-right or Lefty-A	9944
<input type="checkbox"/>	L5	L4 same (cdna or c-dna or gene or genetically or genetic or genes or mrna or clone or plasmid or coding or orf or seq or nucleic or nucleotide or polynucleotide or poly-nucleic or poly-nucleotide or nuclear or chromosomal or chromosome)	157
<input type="checkbox"/>	L6	L5 not l3	109
<input type="checkbox"/>	L7	l6 and tgf	41
<input type="checkbox"/>	L8	l6 and tgfb	6
<input type="checkbox"/>	L9	l6 and tgfbeta	0
<input type="checkbox"/>	L10	l6 and tgf-beta	38
<input type="checkbox"/>	L11	l6 and tgf-beta4	0
<input type="checkbox"/>	L12	l6 and tgf-b-4	0
<input type="checkbox"/>	L13	l6 and tgf-b4	0
<input type="checkbox"/>	L14	l8 or l10	39
<input type="checkbox"/>	L15	l8 or l10	39
<input type="checkbox"/>	L16	L15 not l3	39

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<input type="checkbox"/>	L1	eabf	179
<input type="checkbox"/>	L2	L1 and human	155
<input type="checkbox"/>	L3	l1 same human	124
<input type="checkbox"/>	L4	Tabibzadehin.	0
<input type="checkbox"/>	L5	Tabibzadehin.in.	0
<input type="checkbox"/>	L6	tabibzadeh.in.	23

END OF SEARCH HISTORY

1. 20060099576. 11 Dec 01. 11 May 06. Method for diagnosing a pre-neoplastic or neoplastic lesion in transitional epithelial cells. Tabibzadeh; Siamak. 435/6; 435/7.23 C12Q1/68 20060101 G01N33/574 20060101

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☐ 2. 20030032047. 26 Jul 02. 13 Feb 03. Method for diagnosing selected adenocarcinomas. Tabibzadeh, Siamak. 435/6; C12Q001/68 G01N033/53.

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☐ 3. 6747004. 28 Apr 00; 08 Jun 04. Method for inducing growth and enhancing survival of nervous tissue. Tabibzadeh; Siamak. 514/12; 435/375 514/1 514/2 514/44. A61K038/00 A01N061/00 A01N037/18 C12N005/00 .

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☐ 4. 6683156. 16 Mar 00; 27 Jan 04. Method for diagnosing selected adenocarcinomas. Tabibzadeh; Siamak. 530/350; 530/351 530/399 536/23.1 536/23.5. C07K017/00 C07H021/04 .

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☐ 5. 6649588. 05 Oct 00; 18 Nov 03. Inhibition of TGF-.beta. and uses thereof. Tabibzadeh; Siamak, et al. 514/2; 514/21 514/899 530/350. A61K038/00 A01N025/00 C07K017/00 .

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☐ 6. 6294662. 29 Jun 99; 25 Sep 01. Nucleic acids encoding an endometrial bleeding associated factor (ebaf). Tabibzadeh; Siamak. 536/23.5; 435/6 536/23.1 536/24.31 536/24.33. C07H021/04 C12Q001/68 .

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☐ 7. 5916751. 27 Aug 97; 29 Jun 99. Method for the diagnosis of selected adenocarcinomas. Tabibzadeh; Siamak, et al. 435/6; 435/7.23 436/64 436/813. G01N033/574 G01N033/48 C12Q001/68 .

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☐ 8. 5338164. 28 May 93; 16 Aug 94. Positive displacement micropump. Sutton; Robert F., et al. 417/413.2; F04B017/00 .

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☐ 9. 5171432. 05 Mar 91; 15 Dec 92. Liquid and particle separator. Tabibzadeh; Manouchehr. 210/94; 210/256 210/298 210/299 210/416.1. B01D029/64 .

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☐ 10. WO009955902A1. 29 Apr 99. 04 Nov 99. DIAGNOSTIC MARKERS OF HUMAN FEMALE INFERTILITY. TABIBZADEH, SIAMAK. C12Q001/00;.

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☐ 11. US20060099576A. Determining whether subject has pre-neoplastic/neoplastic lesion in transitional epithelial cells, by assaying diagnostic sample of subject for endometrial bleeding associated factor ebaf expression, detecting elevated ebaf expression. TABIBZADEH, S. C12Q001/68 G01N033/574.

---

☐ 12. US 6747004B. Inducing growth and/or enhancing survival of embryonic forebrain cells with an endometrial bleeding associated factor (ebaf) protein, useful for Parkinson's disease, Alzheimer's disease and amyotrophic lateral sclerosis. TABIBZADEH, S. A01N037/18 A01N061/00 A61K038/00 C12N005/00.

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☐ 13. US 6683156B. New endometrial bleeding associated factor protein, useful for diagnosing a mucinous adenocarcinoma of the ovaries or colon in a female human or of the testis or colon of a male human. TABIBZADEH, S. C07H021/04 C07K017/00.

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☐ 14. US20030032047A. Diagnosis of, e.g. mucinous colon or testicular adenocarcinomas in humans, by removing a bodily fluid sample from the human, and assaying the sample for elevated expression of specific genes. TABIBZADEH, S. C12Q001/68 G01N033/53.

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- ☐ 15. WO 200234281A. Promoting hair growth in a subject, useful for preventing or treating hair loss and all types of alopecia, comprises administering endometrial bleeding associated factor or its analog, or modulator of their expression. MASON, J M, et al. A61K038/00 C07H021/04.
- 
- ☐ 16. WO 200229105A. Inhibiting the activity of transforming growth factor (TGF) beta, for treating e.g. fibrosis, comprises contacting tissue expressing TGF beta with ebf peptide its analogue. MASON, J M, et al. A01N025/00 A01N037/18 A61K038/00 C07K001/00 C07K014/00 C07K017/00 C12Q001/68 G01N033/574.
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- ☐ 17. US 6294662B. New nucleic acid molecule encoding endometrial bleeding associated factor, useful in early diagnosis of selected adenocarcinomas in human, e.g. adenocarcinomas of colon, ovaries or testis. TABIBZADEH, S. C07H021/04 C12Q001/68.
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- ☐ 18. WO 200101134A. New isolated nucleic acid useful for diagnosing colon, testicular, and ovarian cancer. TABIBZADEH, S. G01N033/53.
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- ☐ 19. WO 200066068A. Inducing growth and enhancing survival of nervous tissue by contacting with endometrial bleeding associated factor protein. TABIBZADEH, S. A01N037/18 A61K000/00 A61K031/05 A61K031/203 A61K031/57 A61K035/76 A61K038/00 A61K045/00 A61K048/00 A61P025/14 A61P025/16 A61P025/28 C07J009/00 C12N005/10 C12N015/09.
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- ☐ 20. WO 9955902A. Diagnosis of endometrial irregularities by detecting ebf or its splice variants, particularly for diagnosing infertility. TABIBZADEH, S. C12Q001/00.
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- ☐ 21. US 5916751A. Detecting serous or mucinous colon/ovarian adenocarcinomas and testicular adenocarcinoma by assaying for elevated expression of a gene. KOTHAPALLI, R, et al. C12Q001/68 G01N033/48 G01N033/574.
- 
- ☐ 22. US 5338164A. Positive displacement micro-pump - has series of chambers in stack where electrodeformable material is used to deform diaphragm to change volume in chambers. LANG, K, et al. F04B017/00.
- 
- ☐ 23. US 5171432A. Liq. and particle separator for sewage treatment, etc. - comprises movable piston in vertical cylinder and particle filter fixed inside removable conical tank connected to top of cylinder. TABIBZADEH, M. B01D029/64.
- 

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E3	4	*TGFB4
E4	1	TGFC
E5	2	TGFCYS33SER
E6	1	TGFD
E7	1	TGFDE
E8	13	TGFE
E9	1	TGFFBETA1
E10	1	TGFG
E11	1	TGFGF
E12	2	TGFGF2

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? e transforming growth factor beta 4

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E3	0		*TRANSFORMING GROWTH FACTOR BETA 4
E4	3377		TRANSFORMING GROWTH FACTOR BETA1
E5	3		TRANSFORMING GROWTH FACTOR BETA1 (41-65)
E6	408		TRANSFORMING GROWTH FACTOR BETA2
E7	222		TRANSFORMING GROWTH FACTOR BETA3
E8	6		TRANSFORMING GROWTH FACTOR BETA4
E9	4		TRANSFORMING GROWTH FACTOR BETA5
E10	20		TRANSFORMING GROWTH FACTOR TYPE ALPHA-PSEUDOMO
E11	4		TRANSFORMING GROWTH FACTOR TYPE E
E12	2		TRANSFORMING GROWTH FACTOR (ALPHA)-PSEUDOMONAS

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S2 6 'TRANSFORMING GROWTH FACTOR BETA4'

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Ref	Items	RT	Index-term
E13	1		TRANSFORMING GROWTH FACTOR-ALPHA (8-50)
E14	823		TRANSFORMING GROWTH FACTOR-BETA TYPE II RECEPT
E15	2189	7	TRANSFORMING GROWTH FACTORS
E16	15		TRANSFORMING GROWTH FACTORS --ADMINISTRATION A
E17	1		TRANSFORMING GROWTH FACTORS --ADVERSE EFFECTS
E18	83		TRANSFORMING GROWTH FACTORS --ANALYSIS --AN
E19	16		TRANSFORMING GROWTH FACTORS --ANTAGONISTS AND
E20	122		TRANSFORMING GROWTH FACTORS --BIOSYNTHESIS --B
E21	15		TRANSFORMING GROWTH FACTORS --BLOOD --BL
E22	2		TRANSFORMING GROWTH FACTORS --CHEMICAL SYNTHES
E23	11		TRANSFORMING GROWTH FACTORS --CHEMISTRY --CH
E24	7		TRANSFORMING GROWTH FACTORS --CLASSIFICATION -

Enter P or PAGE for more

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Ref	Items	Type	RT	Index-term
R1	2189		7	*TRANSFORMING GROWTH FACTORS
R2	2189	X		DC=D12.644.276.984. (TRANSFORMING GROWTH FACTORS)
R3	2189	X		DC=D23.348.479.992. (TRANSFORMING GROWTH FACTORS)



Ref	Items	Type	RT	Index-term
R4	2189	X		DC=D23.348.900. (TRANSFORMING GROWTH FACTORS)
R5	22103	B	210	GROWTH SUBSTANCES
R6	6845	B	159	INTERCELLULAR SIGNALING PEPTIDES AND PROTEINS
R7	3189	N	6	TRANSFORMING GROWTH FACTOR ALPHA
R8	23545	N	10	TRANSFORMING GROWTH FACTOR BETA

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Ref	Items	Type	RT	Index-term
R1	23545		10	*TRANSFORMING GROWTH FACTOR BETA
R2	23545	X		DC=D12.644.276.174.400.800. (TRANSFORMING GROWTH FACTOR BETA)
R3	23545	X		DC=D12.644.276.984.720. (TRANSFORMING GROWTH FACTOR BETA)
R4	23545	X		DC=D12.776.467.374.400.800. (TRANSFORMING GROWTH FACTOR BETA)
R5	23545	X		DC=D23.348.479.992.720. (TRANSFORMING GROWTH FACTOR BETA)
R6	23545	X		DC=D23.348.900.720. (TRANSFORMING GROWTH FACTOR BETA)
R7	0	X	1	BONE-DERIVED TRANSFORMING GROWTH FACTOR
R8	0	X	1	PLATELET TRANSFORMING GROWTH FACTOR
R9	1	X	1	TGF-BETA
R10	22103	B	210	GROWTH SUBSTANCES
R11	2189	B	7	TRANSFORMING GROWTH FACTORS

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 >>>Related terms display completed...  
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Ref	Items	RT	Index-term
E1	0	1	TRANSFORMING GROWTH FACTOR ALPHA RECEPTOR
E2	12		TRANSFORMING GROWTH FACTOR ALPHA-PSEUDOMONAS E
E3	23545	10	*TRANSFORMING GROWTH FACTOR BETA
E4	379		TRANSFORMING GROWTH FACTOR BETA --ADMINISTRATI
E5	37		TRANSFORMING GROWTH FACTOR BETA --ADVERSE EFFE
E6	11		TRANSFORMING GROWTH FACTOR BETA --AGONISTS --A
E7	1299		TRANSFORMING GROWTH FACTOR BETA --ANALYSIS --A
E8	795		TRANSFORMING GROWTH FACTOR BETA --ANTAGONISTS
E9	2301		TRANSFORMING GROWTH FACTOR BETA --BIOSYNTHESIS
E10	809		TRANSFORMING GROWTH FACTOR BETA --BLOOD --BL
E11	45		TRANSFORMING GROWTH FACTOR BETA --CEREBROSPINA
E12	1		TRANSFORMING GROWTH FACTOR BETA --CHEMICAL SYN

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Ref	Items	Type	RT	Index-term
R1	23545		10	*TRANSFORMING GROWTH FACTOR BETA
R2	23545	X		DC=D12.644.276.174.400.800. (TRANSFORMING GROWTH FACTOR BETA)
R3	23545	X		DC=D12.644.276.984.720. (TRANSFORMING GROWTH FACTOR BETA)
R4	23545	X		DC=D12.776.467.374.400.800. (TRANSFORMING GROWTH FACTOR BETA)
R5	23545	X		DC=D23.348.479.992.720. (TRANSFORMING GROWTH FACTOR BETA)
R6	23545	X		DC=D23.348.900.720. (TRANSFORMING GROWTH FACTOR BETA)
R7	0	X	1	BONE-DERIVED TRANSFORMING GROWTH FACTOR
R8	0	X	1	PLATELET TRANSFORMING GROWTH FACTOR
R9	1	X	1	TGF-BETA
R10	22103	B	210	GROWTH SUBSTANCES
R11	2189	B	7	TRANSFORMING GROWTH FACTORS

? e r11

Ref	Items	Type	RT	Index-term
R1	2189		7	*TRANSFORMING GROWTH FACTORS
R2	2189	X		DC=D12.644.276.984. (TRANSFORMING GROWTH FACTORS)
R3	2189	X		DC=D23.348.479.992. (TRANSFORMING GROWTH FACTORS)
R4	2189	X		DC=D23.348.900. (TRANSFORMING GROWTH FACTORS)
R5	22103	B	210	GROWTH SUBSTANCES
R6	6845	B	159	INTERCELLULAR SIGNALING PEPTIDES AND PROTEINS
R7	3189	N	6	TRANSFORMING GROWTH FACTOR ALPHA
R8	23545	N	10	TRANSFORMING GROWTH FACTOR BETA

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>>>Related terms display completed...

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Ref	Items	Type	RT	Index-term
R1	23545		10	*TRANSFORMING GROWTH FACTOR BETA
R2	23545	X		DC=D12.644.276.174.400.800. (TRANSFORMING GROWTH FACTOR BETA)
R3	23545	X		DC=D12.644.276.984.720. (TRANSFORMING GROWTH FACTOR BETA)
R4	23545	X		DC=D12.776.467.374.400.800. (TRANSFORMING GROWTH FACTOR BETA)
R5	23545	X		DC=D23.348.479.992.720. (TRANSFORMING GROWTH FACTOR BETA)
R6	23545	X		DC=D23.348.900.720. (TRANSFORMING GROWTH FACTOR BETA)
R7	0	X	1	BONE-DERIVED TRANSFORMING GROWTH FACTOR
R8	0	X	1	PLATELET TRANSFORMING GROWTH FACTOR
R9	1	X	1	TGF-BETA
R10	22103	B	210	GROWTH SUBSTANCES
R11	2189	B	7	TRANSFORMING GROWTH FACTORS

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Ref	Items	Type	RT	Index-term
R1	1		1	*TGF-BETA
R2	23545	X	10	TRANSFORMING GROWTH FACTOR BETA

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Ref	Items	Index-term
E1	1	TRANSFORMER
E2	5	TRANSFORMING
E3	0	*TRANSFORMING GROWTH FACTOR BETA
E4	1	TRANSFORMS
E5	1	TRANSFS
E6	1	TRANSFUZIONNYKH
E7	1	TRANSFUSATE
E8	12	TRANSFUSED
E9	1	TRANSFUSIJSKO
E10	1	TRANSFUSING
E11	2	TRANSFUSIO
E12	1	TRANSFUSIOLOGIST

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Ref	Items	RT	Index-term
E1	0	1	TRANSFORMING GROWTH FACTOR ALPHA RECEPTOR
E2	12		TRANSFORMING GROWTH FACTOR ALPHA-PSEUDOMONAS E
E3	23545	10	*TRANSFORMING GROWTH FACTOR BETA
E4	379		TRANSFORMING GROWTH FACTOR BETA --ADMINISTRATI
E5	37		TRANSFORMING GROWTH FACTOR BETA --ADVERSE EFFE
E6	11		TRANSFORMING GROWTH FACTOR BETA --AGONISTS --A

E7	1299	TRANSFORMING GROWTH FACTOR BETA --ANALYSIS --A
E8	795	TRANSFORMING GROWTH FACTOR BETA --ANTAGONISTS
E9	2301	TRANSFORMING GROWTH FACTOR BETA --BIOSYNTHESIS
E10	809	TRANSFORMING GROWTH FACTOR BETA --BLOOD --BL
E11	45	TRANSFORMING GROWTH FACTOR BETA --CEREBROSPINA
E12	1	TRANSFORMING GROWTH FACTOR BETA --CHEMICAL SYN

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Ref	Items	Index-term
E13	328	TRANSFORMING GROWTH FACTOR BETA --CHEMISTRY --
E14	48	TRANSFORMING GROWTH FACTOR BETA --CLASSIFICATI
E15	101	TRANSFORMING GROWTH FACTOR BETA --DEFICIENCY -
E16	5	TRANSFORMING GROWTH FACTOR BETA --DIAGNOSTIC U
E17	228	TRANSFORMING GROWTH FACTOR BETA --DRUG EFFECTS
E18	4931	TRANSFORMING GROWTH FACTOR BETA --GENETICS --G
E19	1	TRANSFORMING GROWTH FACTOR BETA --HISTORY --HI
E20	1008	TRANSFORMING GROWTH FACTOR BETA --IMMUNOLOGY -
E21	98	TRANSFORMING GROWTH FACTOR BETA --ISOLATION AN
E22	5792	TRANSFORMING GROWTH FACTOR BETA --METABOLISM -
E23	29	TRANSFORMING GROWTH FACTOR BETA --PHARMACOKINE
E24	6920	TRANSFORMING GROWTH FACTOR BETA --PHARMACOLOGY

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Ref	Items	RT	Index-term
E25	3828		TRANSFORMING GROWTH FACTOR BETA --PHYSIOLOGY -
E26	27		TRANSFORMING GROWTH FACTOR BETA --RADIATION EF
E27	376		TRANSFORMING GROWTH FACTOR BETA --SECRETION --
E28	2		TRANSFORMING GROWTH FACTOR BETA --STANDARDS --
E29	370		TRANSFORMING GROWTH FACTOR BETA --THERAPEUTIC
E30	36		TRANSFORMING GROWTH FACTOR BETA --TOXICITY --T
E31	78		TRANSFORMING GROWTH FACTOR BETA --URINE --UR
E32	2675		TRANSFORMING GROWTH FACTOR BETA //RECEPTORS, (RECEPTORS,
			TRANSFORMING GROWTH FACTOR BETA)
E33	6		TRANSFORMING GROWTH FACTOR BETA MASKING PROTEI
E34	31		TRANSFORMING GROWTH FACTOR BETA PRECURSOR
E35	0	1	TRANSFORMING GROWTH FACTOR BETA RECEPTORS
E36	1		TRANSFORMING GROWTH FACTOR BETA 1 LATENCY ASSO

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Ref	Items	RT	Index-term
E37	3377		TRANSFORMING GROWTH FACTOR BETA1
E38	3		TRANSFORMING GROWTH FACTOR BETA1 (41-65)
E39	408		TRANSFORMING GROWTH FACTOR BETA2
E40	222		TRANSFORMING GROWTH FACTOR BETA3
E41	6		TRANSFORMING GROWTH FACTOR BETA4
E42	4		TRANSFORMING GROWTH FACTOR BETA5
E43	20		TRANSFORMING GROWTH FACTOR TYPE ALPHA-PSEUDOMO
E44	4		TRANSFORMING GROWTH FACTOR TYPE E
E45	2		TRANSFORMING GROWTH FACTOR(ALPHA)-PSEUDOMONAS
E46	1		TRANSFORMING GROWTH FACTOR-ALPHA (8-50)
E47	823		TRANSFORMING GROWTH FACTOR-BETA TYPE II RECEPT
E48	2189	7	TRANSFORMING GROWTH FACTORS

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Ref	Items	Index-term
E49	15	TRANSFORMING GROWTH FACTORS --ADMINISTRATION A
E50	1	TRANSFORMING GROWTH FACTORS --ADVERSE EFFECTS

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Ref	Items	Index-term
E1	1	TRANSFORMING GROWTH FACTORS --ADVERSE EFFECTS
E2	83	TRANSFORMING GROWTH FACTORS --ANALYSIS --AN
E3	16	TRANSFORMING GROWTH FACTORS --ANTAGONISTS AND
E4	122	TRANSFORMING GROWTH FACTORS --BIOSYNTHESIS --B
E5	15	TRANSFORMING GROWTH FACTORS --BLOOD --BL
E6	2	TRANSFORMING GROWTH FACTORS --CHEMICAL SYNTHES
E7	11	TRANSFORMING GROWTH FACTORS --CHEMISTRY --CH
E8	7	TRANSFORMING GROWTH FACTORS --CLASSIFICATION -
E9	1	TRANSFORMING GROWTH FACTORS --DEFICIENCY --DF
E10	1	TRANSFORMING GROWTH FACTORS --DIAGNOSTIC USE -
E11	7	TRANSFORMING GROWTH FACTORS --DRUG EFFECTS --D
E12	297	TRANSFORMING GROWTH FACTORS --GENETICS --GE

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Ref	Items	Index-term
E13	1	TRANSFORMING GROWTH FACTORS --HISTORY --HI
E14	49	TRANSFORMING GROWTH FACTORS --IMMUNOLOGY --IM
E15	40	TRANSFORMING GROWTH FACTORS --ISOLATION AND PU
E16	236	TRANSFORMING GROWTH FACTORS --METABOLISM --ME
E17	1	TRANSFORMING GROWTH FACTORS --PHARMACOKINETICS
E18	571	TRANSFORMING GROWTH FACTORS --PHARMACOLOGY --P
E19	324	TRANSFORMING GROWTH FACTORS --PHYSIOLOGY --PH
E20	26	TRANSFORMING GROWTH FACTORS --SECRETION --SE
E21	20	TRANSFORMING GROWTH FACTORS --THERAPEUTIC USE
E22	2	TRANSFORMING GROWTH FACTORS --TOXICITY --TO
E23	7	TRANSFORMING GROWTH FACTORS --URINE --UR
E24	2	TRANSFORMING IMMORTALIZED MAMMARY PROTEIN, HUM

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Ref	Items	Index-term
E25	1	TRANSFORMINNG
E26	1	TRANSFORMION
E27	1	TRANSFORMIRAN
E28	1	TRANSFORMIRANIM
E29	1	TRANSFORMIROVANNKH
E30	1	TRANSFORMIROVANNOG
E31	4	TRANSFORMIROVANNOGO
E32	8	TRANSFORMIROVANNOI
E33	3	TRANSFORMIROVANNOM
E34	9	TRANSFORMIROVANNYE
E35	204	TRANSFORMIROVANNYKH
E36	2	TRANSFORMIROVANNYM

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Set	Items	Description
S1	4	'TGFB4'
S2	6	'TRANSFORMING GROWTH FACTOR BETA4'

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? s s1 or s2
      4 S1
      6 S2
      S3 10 S1 OR S2
? s s3/1997:2006
      10 S3
      5000506 PY=1997 : PY=2006
      S4 10 S3/1997:2006
? b 155 medicine
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      $9.92 2.917 DialUnits File155
      $9.92 Estimated cost File155
      $1.06 TELNET
      $10.98 Estimated cost this search
      $10.98 Estimated total session cost 3.140 DialUnits
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for information about recent updates added to MEDLINE.

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File 172:EMBASE Alert 2006/Jun 23

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Set Items Description  
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Ref	Items	Index-term
E1	1	TGFB3/MSX1 MARKERS
E2	1	TGFB3VARIANT
E3	21	*TGFB4
E4	1	TGFB47
E5	1	TGFB5
E6	8	TGFC
E7	1	TGFCARS
E8	1	TGFCDIA
E9	6	TGFCYS
E10	1	TGFCYSSUP33SER
E11	2	TGFCYS33
E12	3	TGFCYS33SER

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S1 21 'TGFB4'

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Ref	Items	RT	Index-term
E1	2		TRANSFORMING GROWTH FACTOR B-1
E2	1		TRANSFORMING GROWTH FACTOR B-1 TGF-B1
E3	66795	41	*TRANSFORMING GROWTH FACTOR BETA
E4	1		TRANSFORMING GROWTH FACTOR BETA ( TGF-BETA)
E5	1		TRANSFORMING GROWTH FACTOR BETA (TAFB)
E6	1		TRANSFORMING GROWTH FACTOR BETA (TGF BETA 1)
E7	7		TRANSFORMING GROWTH FACTOR BETA (TGF BETA)
E8	1		TRANSFORMING GROWTH FACTOR BETA (TGF)-BETA(1)
E9	1		TRANSFORMING GROWTH FACTOR BETA (TGF- BETA)
E10	51		TRANSFORMING GROWTH FACTOR BETA (TGF-BETA)
E11	1		TRANSFORMING GROWTH FACTOR BETA (TGF-BETA) AND
E12	2		TRANSFORMING GROWTH FACTOR BETA (TGF-BETA) REC

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Ref	Items	Type	RT	Index-term
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R1	60658		41	*TRANSFORMING GROWTH FACTOR BETA
R2	3666	U	2	TGF BETA
R3	14733	X		DC=D11.303.900.720.
R4	27005	X		DC=D12.644.276.174.400.800.
R5	27062	X		DC=D12.644.276.984.720.
R6	14733	X		DC=D12.644.900.720.
R7	27005	X		DC=D12.776.467.374.400.800.
R8	27005	X		DC=D23.348.479.992.720.
R9	27005	X		DC=D23.348.900.720.
R10	0	X	2	BONE-DERIVED TRANSFORMING GROWTH FACTOR
R11	0	X	2	PLATELET TRANSFORMING GROWTH FACTOR
R12	7	X	2	TGF-BETA

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Ref	Items	Type	RT	Index-term
R13	25046	B	420	GROWTH SUBSTANCES
R14	2477	B	14	TRANSFORMING GROWTH FACTORS
R15	14733	X		DC=D24.185.348.900.720.
R16	299917			DC=D24.35.190
R17	141274			DC=D24.35.540.360
R18	14733	X		DC=D24.611.350.400.800.
R19	0	X	1	BONE-DERIVED TRANSFORMING GROWTH FACTOR
R20	0	X	1	PLATELET TRANSFORMING GROWTH FACTOR
R21	1	X	1	TGF-BETA
R22	18857	B	102	GROWTH SUBSTANCES
R23	1456	B	7	TRANSFORMING GROWTH FACTORS
R24	141274			DC=D29.25.540.360

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Ref	Items	Type	RT	Index-term
R25	299917			DC=D4.680.190
R26	141274			DC=D4.680.360
R27	131074	B	270	CYTOKINE
R28	21001	B	161	GROWTH FACTOR
R29	0	S	1	BETA TRANSFORMING GROWTH FACTOR
R30	0	S	1	PLATELET DERIVED TRANSFORMING GROWTH FACTOR BE
R31	0	S	1	TRANSFORMING GROWTH FACTOR TYPE BETA
R32	0	S	1	TYPE BETA TRANSFORMING GROWTH FACTOR

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>>>Related terms display completed...

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Ref	Items	RT	Index-term
E1	2		TRANSFORMING GROWTH FACTOR B-1
E2	1		TRANSFORMING GROWTH FACTOR B-1 TGF-B1
E3	66795	41	*TRANSFORMING GROWTH FACTOR BETA
E4	1		TRANSFORMING GROWTH FACTOR BETA ( TGF-BETA)
E5	1		TRANSFORMING GROWTH FACTOR BETA (TAFB)
E6	1		TRANSFORMING GROWTH FACTOR BETA (TGF BETA 1)
E7	7		TRANSFORMING GROWTH FACTOR BETA (TGF BETA)
E8	1		TRANSFORMING GROWTH FACTOR BETA (TGF)-BETA(1)
E9	1		TRANSFORMING GROWTH FACTOR BETA (TGF- BETA)
E10	51		TRANSFORMING GROWTH FACTOR BETA (TGF-BETA)
E11	1		TRANSFORMING GROWTH FACTOR BETA (TGF-BETA) AND
E12	2		TRANSFORMING GROWTH FACTOR BETA (TGF-BETA) REC

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      $0.02      0.004 DialUnits File5
$0.02 Estimated cost File5
      $0.09      0.004 DialUnits File34
$0.09 Estimated cost File34
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      $0.01      0.004 DialUnits File94
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$0.01 Estimated cost File164
      $0.04      0.004 DialUnits File172
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      $0.01      0.004 DialUnits File266
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       \$0.05     0.004 DialUnits File399  
 \$0.05 Estimated cost File399  
       \$0.09     0.004 DialUnits File434  
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       \$0.02     0.004 DialUnits File444  
 \$0.02 Estimated cost File444  
       \$0.03     0.004 DialUnits File467  
 \$0.03 Estimated cost File467  
       OneSearch, 25 files, 0.100 DialUnits FileOS  
 \$0.67 Estimated cost this search  
 \$19.81 Estimated total session cost     4.316 DialUnits

SYSTEM:OS - DIALOG OneSearch

File 155:MEDLINE(R) 1951-2006/Jun 20

(c) format only 2006 Dialog

**\*File 155: Please see HELP NEWS 154**

for information about recent updates added to MEDLINE.

File 5:Biosis Previews(R) 1969-2006/Jun W3

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File 34:SciSearch(R) Cited Ref Sci 1990-2006/Jun W3

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File 35:Dissertation Abs Online 1861-2006/Jun

(c) 2006 ProQuest Info&Learning

File 65:Inside Conferences 1993-2006/Jun 23

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File 73:EMBASE 1974-2006/Jun 23

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File 91:MANTIS(TM) 1880-2006/Feb

2006 (c) Action Potential

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File 98:General Sci Abs 1984-2005/Jan

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(c) 2006 NewsRx

File 144:Pascal 1973-2006/May W4

(c) 2006 INIST/CNRS

File 149:TGG Health&Wellness DB(SM) 1976-2006/Jun W1

(c) 2006 The Gale Group

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(c) format only 2006 Dialog

**\*File 156: ToxFile has been reloaded. Accession numbers have changed.**

File 159:Cancerlit 1975-2002/Oct

(c) format only 2002 Dialog

**\*File 159: Cancerlit is no longer updating.**

Please see HELP NEWS159.

File 162:Global Health 1983-2006/May

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File 164:Allied & Complementary Medicine 1984-2006/Jun

(c) 2006 BLHCIS

File 172:EMBASE Alert 2006/Jun 23

(c) 2006 Elsevier Science B.V.

File 266:FEDRIP 2005/Dec

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(c) 1999 AAAS

**\*File 370: This file is closed (no updates). Use File 47 for more current information.**

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(c) 2006 American Chemical Society

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IPCR/8 classification codes now searchable as IC=. See HELP NEWSIPCR.

File 434:SciSearch(R) Cited Ref Sci 1974-1989/Dec  
(c) 1998 Inst for Sci Info

File 444:New England Journal of Med. 1985-2006/Jun W2  
(c) 2006 Mass. Med. Soc.

File 467:ExtraMED(tm) 2000/Dec  
(c) 2001 Informania Ltd.

**\*File 467: F467 will close on February 1, 2006.**

7.

Set Items Description

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? e transforming growth factor beta

Ref	Items	RT	Index-term
E1	2		TRANSFORMING GROWTH FACTOR B-1
E2	1		TRANSFORMING GROWTH FACTOR B-1 TGF-B1
E3	66795	41	*TRANSFORMING GROWTH FACTOR BETA
E4	1		TRANSFORMING GROWTH FACTOR BETA ( TGF-BETA)
E5	1		TRANSFORMING GROWTH FACTOR BETA (TAFB)
E6	1		TRANSFORMING GROWTH FACTOR BETA (TGF BETA 1)
E7	7		TRANSFORMING GROWTH FACTOR BETA (TGF BETA)
E8	1		TRANSFORMING GROWTH FACTOR BETA (TGF)-BETA(1)
E9	1		TRANSFORMING GROWTH FACTOR BETA (TGF- BETA)
E10	51		TRANSFORMING GROWTH FACTOR BETA (TGF-BETA)
E11	1		TRANSFORMING GROWTH FACTOR BETA (TGF-BETA) AND
E12	2		TRANSFORMING GROWTH FACTOR BETA (TGF-BETA) REC

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Ref	Items	Index-term
E13	4	TRANSFORMING GROWTH FACTOR BETA (TGF-BETA) SUP
E14	1	TRANSFORMING GROWTH FACTOR BETA (TGF-P) AND PR
E15	1	TRANSFORMING GROWTH FACTOR BETA (TGF-P) SOLUBL
E16	1	TRANSFORMING GROWTH FACTOR BETA (TGFB)
E17	5	TRANSFORMING GROWTH FACTOR BETA (TGFBETA)
E18	1	TRANSFORMING GROWTH FACTOR BETA (TGFBETA1)
E19	661	TRANSFORMING GROWTH FACTOR BETA --ADMINISTRATI
E20	9	TRANSFORMING GROWTH FACTOR BETA --ADVERSE DRUG
E21	68	TRANSFORMING GROWTH FACTOR BETA --ADVERSE EFFE
E22	21	TRANSFORMING GROWTH FACTOR BETA --AGONISTS --A
E23	2387	TRANSFORMING GROWTH FACTOR BETA --ANALYSIS --A
E24	1391	TRANSFORMING GROWTH FACTOR BETA --ANTAGONISTS

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Ref	Items	Index-term
E25	4326	TRANSFORMING GROWTH FACTOR BETA --BIOSYNTHESIS
E26	1384	TRANSFORMING GROWTH FACTOR BETA --BLOOD --BL
E27	3	TRANSFORMING GROWTH FACTOR BETA --BUCCAL DRUG

E28	82	TRANSFORMING GROWTH FACTOR BETA	--CEREBROSPINA
E29	2	TRANSFORMING GROWTH FACTOR BETA	--CHEMICAL SYN
E30	600	TRANSFORMING GROWTH FACTOR BETA	--CHEMISTRY --
E31	93	TRANSFORMING GROWTH FACTOR BETA	--CLASSIFICATI
E32	25	TRANSFORMING GROWTH FACTOR BETA	--CLINICAL TRI
E33	154	TRANSFORMING GROWTH FACTOR BETA	--DEFICIENCY -
E34	9	TRANSFORMING GROWTH FACTOR BETA	--DIAGNOSTIC U
E35	16	TRANSFORMING GROWTH FACTOR BETA	--DRUG ADMINIS
E36	22	TRANSFORMING GROWTH FACTOR BETA	--DRUG ANALYSI

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Ref	Items	Index-term	
E37	205	TRANSFORMING GROWTH FACTOR BETA	--DRUG COMBINA
E38	239	TRANSFORMING GROWTH FACTOR BETA	--DRUG COMPARI
E39	13	TRANSFORMING GROWTH FACTOR BETA	--DRUG CONCENT
E40	111	TRANSFORMING GROWTH FACTOR BETA	--DRUG DEVELOP
E41	179	TRANSFORMING GROWTH FACTOR BETA	--DRUG DOSE --
E42	420	TRANSFORMING GROWTH FACTOR BETA	--DRUG EFFECTS
E43	106	TRANSFORMING GROWTH FACTOR BETA	--DRUG INTERAC
E44	296	TRANSFORMING GROWTH FACTOR BETA	--DRUG THERAPY
E45	27	TRANSFORMING GROWTH FACTOR BETA	--DRUG TOXICIT
E46	10074	TRANSFORMING GROWTH FACTOR BETA	--ENDOGENOUS C
E47	8832	TRANSFORMING GROWTH FACTOR BETA	--GENETICS --G
E48	2	TRANSFORMING GROWTH FACTOR BETA	--HISTORY --HI

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Ref	Items	Index-term	
E49	1842	TRANSFORMING GROWTH FACTOR BETA	--IMMUNOLOGY -
E50	1	TRANSFORMING GROWTH FACTOR BETA	--INTRAARTERIA

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Ref	Items	Index-term	
E1	1	TRANSFORMING GROWTH FACTOR BETA	--INTRAARTERIA
E2	5	TRANSFORMING GROWTH FACTOR BETA	--INTRAARTICUL
E3	1	TRANSFORMING GROWTH FACTOR BETA	--INTRACARDIAC
E4	2	TRANSFORMING GROWTH FACTOR BETA	--INTRACAVERNO
E5	4	TRANSFORMING GROWTH FACTOR BETA	--INTRACEREBRA
E6	1	TRANSFORMING GROWTH FACTOR BETA	--INTRACEREBRO
E7	1	TRANSFORMING GROWTH FACTOR BETA	--INTRACISTERN
E8	1	TRANSFORMING GROWTH FACTOR BETA	--INTRADERMAL
E9	1	TRANSFORMING GROWTH FACTOR BETA	--INTRAGASTRIC
E10	6	TRANSFORMING GROWTH FACTOR BETA	--INTRAMUSCULA
E11	5	TRANSFORMING GROWTH FACTOR BETA	--INTRANASAL D
E12	1	TRANSFORMING GROWTH FACTOR BETA	--INTRAOCULAR

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Ref	Items	Index-term	
E13	4	TRANSFORMING GROWTH FACTOR BETA	--INTRAPERITON
E14	3	TRANSFORMING GROWTH FACTOR BETA	--INTRAPLEURAL
E15	5	TRANSFORMING GROWTH FACTOR BETA	--INTRAVENOUS
E16	201	TRANSFORMING GROWTH FACTOR BETA	--ISOLATION AN
E17	9787	TRANSFORMING GROWTH FACTOR BETA	--METABOLISM -
E18	5	TRANSFORMING GROWTH FACTOR BETA	--ORAL DRUG AD
E19	1	TRANSFORMING GROWTH FACTOR BETA	--PARENTERAL D
E20	81	TRANSFORMING GROWTH FACTOR BETA	--PHARMACEUTIC

E21	3	TRANSFORMING GROWTH FACTOR BETA --PHARMACOECON
E22	66	TRANSFORMING GROWTH FACTOR BETA --PHARMACOKINE
E23	15002	TRANSFORMING GROWTH FACTOR BETA --PHARMACOLOGY
E24	6968	TRANSFORMING GROWTH FACTOR BETA --PHYSIOLOGY -

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Ref	Items	Index-term
E25	63	TRANSFORMING GROWTH FACTOR BETA --RADIATION EF
E26	700	TRANSFORMING GROWTH FACTOR BETA --SECRETION --
E27	4	TRANSFORMING GROWTH FACTOR BETA --STANDARDS --
E28	5	TRANSFORMING GROWTH FACTOR BETA --SUBCUTANEOUS
E29	639	TRANSFORMING GROWTH FACTOR BETA --THERAPEUTIC
E30	13	TRANSFORMING GROWTH FACTOR BETA --TOPICAL DRUG
E31	102	TRANSFORMING GROWTH FACTOR BETA --TOXICITY --T
E32	134	TRANSFORMING GROWTH FACTOR BETA --URINE --UR
E33	4699	TRANSFORMING GROWTH FACTOR BETA //RECEPTORS,
E34	1	TRANSFORMING GROWTH FACTOR BETA ACTIVATED
E35	1	TRANSFORMING GROWTH FACTOR BETA ACTIVATED BIND
E36	1	TRANSFORMING GROWTH FACTOR BETA ACTIVATED KIAN

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E37	112	6	TRANSFORMING GROWTH FACTOR BETA ACTIVATED KINA
E38	3		TRANSFORMING GROWTH FACTOR BETA ACTIVATED PROT
E39	1		TRANSFORMING GROWTH FACTOR BETA ACTIVATING KIN
E40	3		TRANSFORMING GROWTH FACTOR BETA ACTIVATION
E41	1		TRANSFORMING GROWTH FACTOR BETA ACTIVATOR PROT
E42	1		TRANSFORMING GROWTH FACTOR BETA ACTIVIN
E43	1		TRANSFORMING GROWTH FACTOR BETA ACTIVIN RECEPT
E44	1		TRANSFORMING GROWTH FACTOR BETA ACTIVIN RESPON
E45	1		TRANSFORMING GROWTH FACTOR BETA ACTIVITY
E46	1		TRANSFORMING GROWTH FACTOR BETA ALPHA
E47	11		TRANSFORMING GROWTH FACTOR BETA ANTAGONIST
E48	263	8	TRANSFORMING GROWTH FACTOR BETA ANTIBODY

Enter P or PAGE for more

? s e48

S2 263 'TRANSFORMING GROWTH FACTOR BETA ANTIBODY'

? s s2/1997:2006

Processing

Processed 10 of 25 files ...

Processing

>>>One or more prefixes are unsupported

>>> or undefined in one or more files.

>>>Year ranges not supported in one or more files

Processed 20 of 25 files ...

Completed processing all files

263 S2

49018771 PY=1997 : PY=2006

S3 246 S2/1997:2006

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263 S2

246 S3

S4 17 S2 NOT S3

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S5 17 RD (unique items)

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Terminal set to DLINK  
? t s5/9/all

Set	Items	Description
S1	21	'TGFB4'
S2	263	'TRANSFORMING GROWTH FACTOR BETA ANTIBODY'
S3	246	S2/1997:2006
S4	17	S2 NOT S3
S5	17	RD (unique items)
S6	125	E1-E8
S7	15	'TRANSFORMING GROWTH FACTOR BETA CDNA' OR E20-E26
S8	6	E13-E16
S9	3	'TRANSFORMING GROWTH FACTOR BETA NEUTRALIZING A'
S10	36	E2-E6
S11	3	'TRANSFORMING GROWTH FACTOR BETA 1 ANTIBODY'
S12	5	E34-E36
S13	1	'TRANSFORMING GROWTH FACTOR BETA 4 GENE'
S14	2	E39-E40
S15	18	'TRANSFORMING GROWTH FACTOR BETA4'
S16	1	'TRANSFORMING GROWTH FACTOR B4'
S17	215	S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16
S18	201	S17/1997:2006
S19	14	S17 NOT S18
S20	31	S19 OR S4
S21	26	RD (unique items)
S22	6	'LEFTA'
S23	36	E3-E4
S24	42	S22 OR S23
S25	42	S24/1997:2006

? logoff hold

5/9/1 (Item 1 from file: 73)

DIALOG(R)File 73:EMBASE

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06761297 EMBASE No: 1997042786

**Transforming growth factor beta in diabetic nephropathy**

Border W.A.; Yamamoto T.; Noble N.A.

W.A. Border, Division of Nephrology, Univ. of Utah School of Medicine, 50 North Medical Drive, Salt Lake City, UT 84132 United States

Diabetes/Metabolism Reviews ( DIABETES METAB. REV. ) (United Kingdom) 1996, 12/4 (309-339)

CODEN: DMREE ISSN: 0742-4221

DOCUMENT TYPE: Journal; Review

LANGUAGE: ENGLISH

NUMBER OF REFERENCES: 128

**DRUG DESCRIPTORS:**

\*angiotensin--endogenous compound--ec; \*antibody--pharmacology--pd; \*antisense oligonucleotide--pharmacology--pd; \*decorin--pharmacology--pd; \*matrix protein--endogenous compound--ec; \*receptor blocking agent--pharmacology--pd; \*transforming growth factor beta--endogenous compound--ec

unclassified drug

**MEDICAL DESCRIPTORS:**

\*diabetic nephropathy--etiology--et  
fibrogenesis; gene therapy; glomerulonephritis--etiology--et; glucose blood level; human; kidney cell; nonhuman; priority journal; review; wound healing

DRUG TERMS (UNCONTROLLED): transforming growth factor beta antagonist

--pharmacology--pd; **transforming growth factor beta antibody**

--pharmacology--pd  
CAS REGISTRY NO.: 11128-99-7, 1407-47-2 (angiotensin)  
SECTION HEADINGS:  
003 Endocrinology  
006 Internal Medicine  
026 Immunology, Serology and Transplantation  
028 Urology and Nephrology  
048 Gastroenterology  
030 Clinical and Experimental Pharmacology  
037 Drug Literature Index

5/9/2 (Item 2 from file: 73)  
DIALOG(R)File 73:EMBASE  
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06717049 EMBASE No: 1996190191

**Marked diversity in the action of growth factors on  
N-methyl-D-aspartate-induced neuronal degeneration**

Prehn J.H.M.

J.H.M. Prehn, Dept. of Pharmacology and Toxicology, Philipps-University,  
Ketzerbach 63, D-35052 Marburg Germany

European Journal of Pharmacology ( EUR. J. PHARMACOL. ) (Netherlands)  
1996, 306/1-3 (81-88)

CODEN: EJPHA ISSN: 0014-2999

DOCUMENT TYPE: Journal; Article

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Neuronal degeneration was induced in cultured rat hippocampal neurons by a 20-min exposure to the glutamatergic agonist, N-methyl-D-aspartate (NMDA; 100  $\mu$ M), and the neuroprotective activity of a set of growth factors and cytokines was compared. During the early stages of degeneration, NMDA induced changes that were characteristic of neuronal necrosis, including swelling and darkening of the neuronal soma and swelling of neurites, leading to the formation of beaded varicosities ('blebs'). These changes were followed by nuclear pyknosis, formation of double-stranded DNA breaks and loss of membrane integrity. Only transforming growth factor-beta1 (TGF-beta1; 1-10 ng/ml) and tumor necrosis factor-alpha (TNF-alpha; 30 ng/ml) protected the hippocampal neurons against NMDA neurotoxicity after short-term (60 min) pre-treatments. Interleukin-1beta (10-100 ng/ml) and fibroblast growth factor-2 (FGF-2; 50 ng/ml) were clearly effective when administered 24 h prior to the NMDA exposure, but not when given 60 min before the insult. Interestingly, the protective effect of interleukin-1beta was significantly reduced in the presence of a neutralizing antibody to TGF-beta. Of note, short-term pre-treatment with brain-derived neurotrophic factor (BDNF; 5-50 ng/ml) significantly potentiated NMDA-induced neurodegeneration. These experiments demonstrate marked diversity in the actions of growth factors on NMDA-induced neuronal degeneration.

MANUFACTURER NAMES: promega/United States; sigma

**DRUG DESCRIPTORS:**

\*cytokine--drug comparison--cm; \*cytokine--pharmacology--pd; \*cytokine  
--drug interaction--it; \*excitotoxin--drug toxicity--to; \*excitotoxin--drug  
interaction--it; \*growth factor--pharmacology--pd; \*growth factor--drug  
interaction--it; \*growth factor--drug comparison--cm; \*n methyl dextro  
aspartic acid--drug interaction--it; \*n methyl dextro aspartic acid--drug  
toxicity--to

glutamate receptor agonist--drug toxicity--to; recombinant epidermal growth  
factor--pharmacology--pd; recombinant epidermal growth factor--drug  
comparison--cm; recombinant fibroblast growth factor--pharmacology--pd;

recombinant fibroblast growth factor--drug interaction--it; recombinant fibroblast growth factor--drug comparison--cm; recombinant interleukin 1beta--pharmacology--pd; recombinant interleukin 1beta--drug interaction--it; recombinant interleukin 1beta--drug comparison--cm; recombinant transforming growth factor beta1--drug interaction--it; recombinant transforming growth factor beta1--drug comparison--cm; recombinant transforming growth factor beta1--pharmacology--pd; unclassified drug  
MEDICAL DESCRIPTORS:

\*hippocampus; \*nerve cell degeneration; \*neuroprotection  
animal cell; article; cell death; cell nucleus; cell structure;  
concentration response; controlled study; dna strand breakage; dose time  
effect relation; drug antagonism; drug potentiation; membrane damage; nerve  
cell culture; neurite; newborn; nonhuman; priority journal; rat  
DRUG TERMS (UNCONTROLLED): recombinant brain derived neurotrophic factor  
--drug interaction--it; recombinant brain derived neurotrophic factor  
--pharmacology--pd; recombinant brain derived neurotrophic factor--drug  
toxicity--to; recombinant brain derived neurotrophic factor--drug  
comparison--cm; **transforming growth factor beta antibody** --pharmacology  
--pd; **transforming growth factor beta antibody** --drug interaction--it  
CAS REGISTRY NO.: 6384-92-5 (n methyl dextro aspartic acid)

SECTION HEADINGS:

- 005 General Pathology and Pathological Anatomy
- 008 Neurology and Neurosurgery
- 026 Immunology, Serology and Transplantation
- 052 Toxicology
- 030 Clinical and Experimental Pharmacology
- 037 Drug Literature Index

5/9/3 (Item 3 from file: 73)

DIALOG(R)File 73:EMBASE

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06421169 EMBASE No: 1996077869

**Transforming growth factor-beta in in vivo resistance**

Teicher B.A.; Holden S.A.; Ara G.; Chen G.

Dana-Farber Cancer Institute, Joint Center for Radiation Therapy, 44

Binney Street, Boston, MA 02115 United States

Cancer Chemotherapy and Pharmacology ( CANCER CHEMOTHER. PHARMACOL. ) ( Germany) 1996, 37/6 (601-609)

CODEN: CCPHD ISSN: 0344-5704

DOCUMENT TYPE: Journal; Article

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

The potential role of transforming growth factor-beta in in vivo resistance was examined by administration of transforming growth factor-beta-neutralizing antibodies to animals bearing the EMT-6/Parent tumor or the antitumor alkylating resistant tumors, EMT-6/CTX or EMT-6/CDDP. Treatment of tumor-bearing animals with anti-TGF-beta antibodies by intraperitoneal injection daily on days 0-8 post-tumor cell implantation increased the sensitivity of the EMT-6/Parent tumor to cyclophosphamide (CTX) and cisplatin (CDDP) and markedly increased the sensitivity of the EMT-6/CTX tumor to CTX and the EMT-6/CDDP tumor to CDDP, as determined by tumor cell survival assay. Bone marrow granulocyte-macrophage colony-forming units (CFU-GM) survival was determined from these same animals. The increase in the sensitivity in the tumors upon treatment with the anti-TGF-beta antibodies was also observed in increased sensitivity of the bone marrow CFU-GM to CTX and CDDP. Treatment of non-tumor-bearing animals with the anti-TGF-beta regimen did not alter blood ATP or serum glucose level but did decrease serum lactate levels. This treatment also decreased hepatic glutathione, glutathione

S-transferase, glutathione reductase, and glutathione peroxidase in non-tumor-bearing animals by 40-60% but increased hepatic cytochrome P450 reductase in these normal animals. Animals bearing the EMT-6/CTX and EMT-6/CDDP tumors had higher serum lactate levels than normal or EMT-6/Parent tumor-bearing animals; these were decreased by the anti-TGF-beta regimen. Treatment of animals bearing any of the three tumors with the anti-TGF-beta regimen decreased by 30-50% the activity of hepatic glutathione S-transferase and glutathione peroxidase, and increased by 35-80% the activity of hepatic cytochrome P450 reductase. In conclusion, treatment with transforming growth factor-beta-neutralizing antibodies restored drug sensitivity in the alkylating agent-resistant tumors, altering both the tumor and host metabolic states.

MANUFACTURER NAMES: genentech/United States; sigma/United States

DRUG DESCRIPTORS:

\*cisplatin--drug therapy--dt; \*cisplatin--drug dose--do; \*cisplatin--drug toxicity--to; \*cisplatin--pharmacology--pd; \*cyclophosphamide--drug toxicity--to; \*cyclophosphamide--drug therapy--dt; \*cyclophosphamide--pharmacology--pd; \*cyclophosphamide--drug dose--do; \*transforming growth factor beta--endogenous compound--ec; adenosine triphosphate--endogenous compound--ec; alkylating agent--pharmacology--pd; antineoplastic agent--pharmacology--pd; cytochrome p450 reductase--endogenous compound--ec; glucose--endogenous compound--ec; glutathione--endogenous compound--ec; glutathione peroxidase--endogenous compound--ec; glutathione reductase--endogenous compound--ec; glutathione transferase--endogenous compound--ec; lactic acid--endogenous compound--ec; neutralizing antibody--drug toxicity--to; neutralizing antibody--drug therapy--dt; neutralizing antibody--pharmacology--pd; unclassified drug

MEDICAL DESCRIPTORS:

\*breast carcinoma--drug therapy--dt; \*breast carcinoma--drug resistance--dr; \*tumor cell; animal cell; animal experiment; animal model; article; blood level; bone marrow toxicity; cancer graft; cell survival; colony forming unit gm; controlled study; drug sensitivity; female; intraperitoneal drug administration; liver level; mouse; nonhuman; priority journal

DRUG TERMS (UNCONTROLLED): **transforming growth factor beta antibody** --drug toxicity--to; **transforming growth factor beta antibody** --pharmacology--pd; **transforming growth factor beta antibody** --drug therapy--dt; **transforming growth factor beta antibody** --drug dose--do

CAS REGISTRY NO.: 15663-27-1, 26035-31-4, 96081-74-2 (cisplatin); 50-18-0 (cyclophosphamide); 15237-44-2, 56-65-5, 987-65-5 (adenosine triphosphate); 9039-06-9, 9075-42-7 (cytochrome p450 reductase); 50-99-7, 84778-64-3 (glucose); 70-18-8 (glutathione); 9013-66-5 (glutathione peroxidase); 9001-48-3 (glutathione reductase); 50812-37-8 (glutathione transferase); 113-21-3, 50-21-5 (lactic acid)

SECTION HEADINGS:

- 016 Cancer
- 025 Hematology
- 026 Immunology, Serology and Transplantation
- 029 Clinical and Experimental Biochemistry
- 052 Toxicology
- 030 Clinical and Experimental Pharmacology
- 037 Drug Literature Index

5/9/4 (Item 4 from file: 73)

DIALOG(R) File 73:EMBASE

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06350226 EMBASE No: 1996003775

Anti-(transforming growth factor beta) antibodies with predefined



**specificity inhibit metastasis of highly tumorigenic human xenotransplants  
in nu/nu mice**

Hoefer M.; Anderer F.A.

Friedrich-Miescher-Laboratorium, Max-Planck-Gesellschaft, Spemannstrasse  
37/39, D-72076 Tübingen Germany

Cancer Immunology Immunotherapy ( CANCER IMMUNOL. IMMUNOTHER. ) (Germany)  
1995, 41/5 (302-308)

CODEN: CIIMD ISSN: 0340-7004

DOCUMENT TYPE: Journal; Article

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Monoclonal antibodies (mAb) were prepared against conjugated transforming growth factor beta1 (TGFbeta1) peptides: amino acid positions 48-60 and positions 86-101. Two antibodies, mAb 16-3G1 (anti(48-60)) and mAb 5-2G6 (anti-(86-101)) cross-reacted with native TGFbeta1, -beta2 and -beta3 (16-3G1) or only with native TGFbeta1 (5-2G6). Both mAb were used to characterize TGFbeta-mediated effects on the metastatic potential in nude mice of human carcinoma cell line SLU-1 and its metastatic subline SLU-M1. Autocrine TGFbeta-mediated up-regulation of cell proliferation and its suppression by anti-TGFbeta antibodies in vitro was recorded for SLU-M1 cells whereas SLU-1 cell proliferation in vitro appeared to be refractory to anti-TGFbeta antibodies and exogenous TGFbeta1. However, the potential of s.c. tumours to develop distant metastases in nude mice was about the same for both cell lines. Development of primary tumours and distant metastases could be suppressed by treatment of mice with anti-TGFbeta antibodies. Thus we assume that the metastatic potential of tumour cells is independent of TGFbeta-mediated growth-regulation effects in vitro. The anti-TGFbeta-induced suppression of tumour progression and metastasis in nude mice might rather result from stimulation of the immune surveillance. TGFbeta-mediated autocrine down-regulation of MHC-unrestricted cytotoxicity of activated human monocytes and CD56sup + LAK cells and its reversion by anti-TGFbeta antibodies could be readily demonstrated. In all our experimental series, the neutralizing potential of both anti-TGFbeta antibodies, though directed against opposite sites of the TGFbeta1 molecule, was very similar.

MANUFACTURER NAMES: biochrom/Germany

DRUG DESCRIPTORS:

\*antimetastatic agent--pharmacology--pd; \*antimetastatic agent--drug  
development--dv; \*monoclonal antibody--pharmacology--pd; \*monoclonal  
antibody--drug development--dv; \*monoclonal antibody--drug dose--do  
unclassified drug

MEDICAL DESCRIPTORS:

\*metastasis potential; \*tumor xenograft  
animal experiment; animal model; article; autocrine effect; controlled  
study; human; human cell; human tissue; intraperitoneal drug administration  
; mouse; nonhuman; priority journal

DRUG TERMS (UNCONTROLLED): **transforming growth factor beta antibody**  
--pharmacology--pd; **transforming growth factor beta antibody** --drug  
development--dv; **transforming growth factor beta antibody** --drug dose--do

SECTION HEADINGS:

016 Cancer  
026 Immunology, Serology and Transplantation  
037 Drug Literature Index

**5/9/5 (Item 5 from file: 73)**

DIALOG(R) File 73:EMBASE

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06155894 EMBASE No: 1995181304

**Perspectives in the treatment of liver fibrosis**

Mavier P.; Mallat A.

Unite d'Hepatology, Hopital Henri-Mondor, 94010 Creteil France

Journal of Hepatology, Supplement ( J. HEPATOL. SUPPL. ) (Denmark) 1995  
22/2 (111-1115)

CODEN: JHSUF ISSN: 0169-5185

DOCUMENT TYPE: Journal; Review

LANGUAGE: ENGLISH

BRAND NAME/MANUFACTURER NAME: hoe 077; s 0885

**DRUG DESCRIPTORS:**

alpha interferon--pharmacology--pd; colchicine--pharmacology--pd;  
colchicine--drug therapy--dt; decorin--pharmacology--pd; gamma interferon  
--pharmacology--pd; glucocorticoid--pharmacology--pd; glucocorticoid--drug  
therapy--dt; lufironil--pharmacology--pd; lufironil--drug therapy--dt;  
penicillamine--drug therapy--dt; penicillamine--pharmacology--pd; retinoid  
--pharmacology--pd; unclassified drug

**MEDICAL DESCRIPTORS:**

\*liver fibrosis--therapy--th; \*liver fibrosis--drug therapy--dt

human; nonhuman; priority journal; review

DRUG TERMS (UNCONTROLLED): s 0885--pharmacology--pd; s 0885--drug therapy  
--dt; **transforming growth factor beta antibody** --pharmacology--pd

CAS REGISTRY NO.: 64-86-8 (colchicine); 82115-62-6 (gamma interferon);  
128075-79-6 (lufironil); 2219-30-9, 52-67-5 (penicillamine)

**SECTION HEADINGS:**

048 Gastroenterology

037 Drug Literature Index

**5/9/6 (Item 6 from file: 73)**

DIALOG(R) File 73:EMBASE

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06046762 EMBASE No: 1995077061

**Expression of tissue-type plasminogen activator and its inhibitor couples with development of capillary network by human microvascular endothelial cells on matrigel**

Ito K.-I.; Ryuto M.; Ushiro S.; Ono M.; Sugeno A.; Kuraoka A.; Shirata Y.; Kuwano M.

Department of Biochemistry, Kyushu University, School of Medicine,  
Maidashi, Fukuoka 812 Japan

Journal of Cellular Physiology ( J. CELL. PHYSIOL. ) (United States)  
1995, 162/2 (213-224)

CODEN: JCLLA ISSN: 0021-9541

DOCUMENT TYPE: Journal; Article

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Human omental microvascular endothelial (HOME) cells seeded on Matrigel begin to migrate within 1 h, forming honeycomb-like structures and capillary-like networks within 18 h. Cross-sections of the capillary networks show them to be tube-like structures. Northern blot analysis showed that tissue-type plasminogen activator (t-PA) mRNA synthesis increased from the initial state at 0 h after seeding on Matrigel, reaching a steady state after 4 h. This elevated cellular t-PA mRNA level decreased markedly at 24 h. In contrast the cellular plasminogen activator inhibitor-1 (PAI-1) mRNA level demonstrated biphasic curves during the 24 h after seeding on Matrigel: the PAI-1 mRNA level was increased eightfold initially at 4 h over that at 0 h, then declined, and again secondarily increased to greater than tenfold at 18 h. Cellular levels of both 72 kD type IV collagenase and tissue inhibitor of metalloproteinase (TIMP-2) mRNA were increased only a slightly within 2-4 h. These elevated mRNA levels were maintained for 18 h, while the TIMP-1 mRNA level increased up to 18 hr

CODEN: THORA ISSN: 0040-6376  
DOCUMENT TYPE: Journal; Editorial  
LANGUAGE: ENGLISH  
DRUG DESCRIPTORS:  
\*antibody--drug therapy--dt; \*transforming growth factor beta  
unclassified drug  
MEDICAL DESCRIPTORS:  
\*fibrosing alveolitis--drug therapy--dt; \*lung fibrosis--drug therapy--dt  
editorial; human; intravenous drug administration; priority journal  
DRUG TERMS (UNCONTROLLED): **transforming growth factor beta antibody** --drug  
therapy--dt  
SECTION HEADINGS:  
015 Chest Diseases, Thoracic Surgery and Tuberculosis  
037 Drug Literature Index

5/9/12 (Item 12 from file: 73)  
DIALOG(R)File 73:EMBASE  
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05428044 EMBASE No: 1993196143  
**The release of transforming growth factor-beta following haemorrhage: Its  
role as a mediator of host immunosuppression**  
Ayala A.; Meldrum D.R.; Perrin M.M.; Chaudry I.H.  
Department of Surgery, Michigan State University, East Lansing, MI 48824  
United States  
Immunology ( IMMUNOLOGY ) (United Kingdom) 1993, 79/3 (479-484)  
CODEN: IMMUA ISSN: 0019-2805  
DOCUMENT TYPE: Journal; Article  
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Haemorrhage in the absence of trauma is reported to induce a profound depression in cell-mediated immunity. Recent studies have drawn attention to the cytokine transforming growth factor-beta (TGF-beta) that, while important in wound healing, also has marked immunosuppressive effects. The aim of this study was to determine whether: (1) haemorrhage induces an increase in circulating TGF-beta and if this is associated with the loss of host immunoresponsiveness; and (2) administration of monoclonal antibody (mAb) to TGF-beta following haemorrhage ablates these changes. To determine this, C3H/HeN mice were bled to and maintained at a mean arterial pressure of 35 mmHg for 1 hr. This required removing ~ 50% of the circulating blood volume. Following this period of hypotension, the mice were adequately resuscitated. Blood samples obtained at 24 and 72 hr, but not at 2 hr, following haemorrhage showed a significant elevation in plasma TGF-beta levels when compared to shams. At 24 hr, the increase of TGF-beta in the plasma was associated with decreases in both concanavalin A (Con A)-induced splenocyte proliferation and splenic macrophage antigen presentation. Treating animals with neutralizing antibody (animals received 200 mug mAb against bovine TGF-beta in 1 ml, 2 ml, 3 ml/mouse intraarterially) not only reduced the levels of TGF-beta in the blood at 24 hr, but also restored splenocyte functions, such as Con A-induced proliferation, interleukin-2 (IL-2) release, and the capacity of splenic macrophages to present antigen. However, elevated levels of prostaglandin E<sub>2</sub> (PGE<sub>2</sub>) seen in plasma during haemorrhage were only partially depressed by the antibody treatment. These results indicate that the release of TGF-beta contributes to the protracted (>=24 hr) suppression of cell-mediated immunity following haemorrhage.

DRUG DESCRIPTORS:  
\*transforming growth factor beta--endogenous compound--ec  
concanavalin a; interleukin 2--endogenous compound--ec; monoclonal antibody

; prostaglandin e2--endogenous compound--ec; unclassified drug

MEDICAL DESCRIPTORS:

\*bleeding; \*immune deficiency; \*immune response; \*mediator  
animal cell; animal model; antigen presentation; article; blood level;  
controlled study; macrophage; male; mediator release; mouse; nonhuman;  
priority journal; spleen cell

DRUG TERMS (UNCONTROLLED): **transforming growth factor beta antibody**  
--pharmacology--pd

CAS REGISTRY NO.: 11028-71-0 (concanavalin a); 85898-30-2 (interleukin 2);  
363-24-6 (prostaglandin e2)

SECTION HEADINGS:

005 General Pathology and Pathological Anatomy  
009 Surgery  
026 Immunology, Serology and Transplantation  
029 Clinical and Experimental Biochemistry  
030 Clinical and Experimental Pharmacology  
037 Drug Literature Index

**5/9/13 (Item 13 from file: 73)**

DIALOG(R) File 73:EMBASE

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05428041 EMBASE No: 1993196140

**Transforming growth factor-beta1 enhances the generation of allospecific cytotoxic T lymphocytes**

Kondo S.; Isobe K.; Ishiguro N.; Nakashima I.; Miura T.  
Dept. of Immunology, Nagoya University School of Medicine, 65  
Tsurumai-cho, Showa-ku, Nagoya 466 Japan  
Immunology ( IMMUNOLOGY ) (United Kingdom) 1993, 79/3 (459-464)  
CODEN: IMMUA ISSN: 0019-2805  
DOCUMENT TYPE: Journal; Article  
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

We investigated the effects of transforming growth factor-beta1 (TGF-beta1) on the proliferation and generation of murine T lymphocytes in vitro. TGF-beta1 suppressed T- and B-lymphocyte proliferation, mixed lymphocyte reaction (MLR), and the generation of natural killer (NK) cells and lymphokine activated killer (LAK) cells. On the other hand, TGF-beta1 significantly enhanced the generation of allospecific cytotoxic T lymphocytes (CTL) at low concentrations (0.01-1 ng/ml) in a dose-dependent manner and restored it to the control level at higher concentrations (10-40 ng/ml). Allospecific CTL generation by TGF-beta1 was maximally enhanced when added at the beginning of culture. Less enhancement occurred when the addition was delayed. Anti-TGF-beta1 antibody completely abolished the enhancing effects of TGF-beta1. Furthermore, platelet-derived TGF-beta (pTGF-beta) as well as recombinant TGF-beta1 similarly enhanced the generation of allospecific CTL. These data demonstrate that TGF-beta has not only immunosuppressive effects but also immuno-enhancing effects in vitro.

MANUFACTURER NAMES: shionogi/Japan

DRUG DESCRIPTORS:

\*transforming growth factor beta1--pharmacology--pd  
antibody--pharmacology--pd; recombinant interleukin 2--pharmacology--pd;  
recombinant transforming growth factor beta1--pharmacology--pd;  
transforming growth factor beta--pharmacology--pd; unclassified drug

MEDICAL DESCRIPTORS:

\*cytotoxic t lymphocyte; \*lymphocyte proliferation  
animal cell; article; b lymphocyte; concentration response; controlled  
study; female; lymphokine activated killer cell; mixed lymphocyte reaction;

CAS REGISTRY NO.: 11128-99-7, 1407-47-2 (angiotensin); 50-23-7 (hydrocortisone)

SECTION HEADINGS:

003 Endocrinology  
037 Drug Literature Index

5/9/16 (Item 16 from file: 73)

DIALOG(R) File 73:EMBASE

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04629371 EMBASE No: 1991123414

**Chondrocytes inhibit endothelial sprout formation in vitro: Evidence for involvement of a transforming growth factor-beta**

Pepper M.S.; Montesano R.; Vassalli J.-D.; Orci L.

Institute of Histology, University of Geneva, Medical Center, 1211 Geneva 4 Switzerland

Journal of Cellular Physiology ( J. CELL. PHYSIOL. ) (United States)  
1991, 146/1 (170-179)

CODEN: JCLLA ISSN: 0021-9541

DOCUMENT TYPE: Journal; Article

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Using a quantitative in vitro model of spontaneous endothelial sprout formation, we have attempted to define physiological inhibitors of angiogenesis from hyaline cartilage, a tissue whose antiangiogenic properties have been well described. The model consists of embedding bovine microvascular endothelial cell aggregates into fibrin or collagen gels, which results in the formation of radially growing sprouts. When chondrocytes derived from the permanent cartilagenous region of the chick embryo sternum are cocultured with the endothelial cell aggregates, sprout formation is markedly inhibited. Addition of anti-TGF-beta antibodies to the cocultures significantly reduces the inhibitory effect of chondrocytes on sprout formation. Chondrocyte-conditioned medium or exogenously added TGF-beta1 have a similar albeit transient inhibitory effect. Depletion of TGF-beta from chondrocyte conditioned medium with anti-TGF-beta antibodies and solid-phase protein-A significantly decreases the inhibition of sprout formation. These results demonstrate that a chondrocyte-derived TGF-beta-like molecule inhibits capillary sprout formation in vitro and suggest that the antiangiogenic properties of cartilage may at least in part, be mediated by TGF-beta.

DRUG DESCRIPTORS:

\*transforming growth factor beta1--endogenous compound--ec  
unclassified drug

MEDICAL DESCRIPTORS:

\*cell growth; \*microvasculature; \*vascular endothelium

animal cell; article; controlled study; cow; nonhuman; priority journal

DRUG TERMS (UNCONTROLLED): **transforming growth factor beta antibody**

--endogenous compound--ec

SECTION HEADINGS:

002 Physiology

5/9/17 (Item 17 from file: 73)

DIALOG(R) File 73:EMBASE

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03315759 EMBASE No: 1987068336

**Transforming growth factor-beta. A very potent inhibitor of myoblast differentiation, identical to the differentiation inhibitor secreted by**

# Buffalo rat liver cells

Florini J.R.; Roberts A.B.; Ewton D.Z.; et al.

Biology Department, Syracuse University, Syracuse, NY 13210 United States

Journal of Biological Chemistry ( J. BIOL. CHEM. ) (United States) 1986 , 261/35 (16509-16513)

CODEN: JBCHA

DOCUMENT TYPE: Journal

LANGUAGE: ENGLISH

Transforming growth factor-beta (TGF-beta) is now known to have a number of actions in addition to the induction of phenotypic transformation in fibroblastic cells. In this paper, we characterize its inhibition of differentiation in rat myoblasts of Yaffe's L6 strain and demonstrate its identity or very close similarity to the differentiation inhibitor (DI) secreted by Buffalo rat liver cells cultured in serum-free medium. At concentrations as low as 60 pg/ml, TGF-beta gave detectable inhibition of differentiation measured as myoblast fusion and creatine kinase elevation; maximal inhibition was observed at and above 0.5 ng/ml (20 pM). The inhibition persisted as long as fresh TGF-beta was added at 48-h intervals, but it was reversed upon removal of the factor. By itself or in the presence of mitogens, TGF-beta had no mitogenic activity in the L6 cells. Concentration dependencies of human TGF-beta and the rat DI were closely parallel in three assays: inhibition of myoblast differentiation, stimulation of normal rat kidney cell growth in soft agar, and competition for displacement of labeled TGF-beta from binding sites on A549 human lung carcinoma cells. We conclude that most if not all of the DI activity found in medium conditioned by Buffalo rat liver cells can be attributed to the presence of TGF-beta or a very similar molecule. These observations also offer a potentially useful approach to study the control of myogenesis; the process(es) can be blocked in cloned L6 myoblasts by incubation with very small quantities of a pure protein in fully defined serum-free medium.

## DRUG DESCRIPTORS:

\*creatine kinase; \*transforming growth factor beta  
radioisotope; unclassified drug

## MEDICAL DESCRIPTORS:

\*cell differentiation; \*cell fusion; \*dose response; \*drug comparison; \*  
drug identification; \*drug isolation; \*drug mechanism; \*drug receptor  
binding; \*drug screening; \*myoblast  
liver cell; rat; priority journal; drug analysis; pharmacokinetics; drug  
response; human cell; animal cell; in vitro study; histology; human; normal  
human; blood and hemopoietic system; respiratory system; liver

DRUG TERMS (UNCONTROLLED): differentiation inhibitor; **transforming growth factor beta antibody** ; transforming growth factor beta i 125

CAS REGISTRY NO.: 9001-15-4 (creatine kinase)

## SECTION HEADINGS:

037 Drug Literature Index  
029 Clinical and Experimental Biochemistry  
021 Developmental Biology and Teratology  
016 Cancer

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23jun06 13:46:27 User228206 Session D2614.6

\$0.03 0.009 DialUnits File155  
\$0.03 Estimated cost File155  
\$0.06 0.009 DialUnits File5  
\$0.06 Estimated cost File5  
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\$0.04 0.009 DialUnits File35  
\$0.04 Estimated cost File35

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<input type="checkbox"/>	L1	ebaf	179
<input type="checkbox"/>	L2	L1 and human	155
<input type="checkbox"/>	L3	l1 same human	124
<input type="checkbox"/>	L4	Tabibzadehin.	0
<input type="checkbox"/>	L5	Tabibzadehin.in.	0
<input type="checkbox"/>	L6	tabibzadeh.in.	23
<input type="checkbox"/>	L7	l1 not l2	24
<input type="checkbox"/>	L8	tgfb-4	6
<input type="checkbox"/>	L9	tgf-b-4	0
<input type="checkbox"/>	L10	tgf-b4	5
<input type="checkbox"/>	L11	tgf-beta4	14
<input type="checkbox"/>	L12	tgf-beta-4	9
<input type="checkbox"/>	L13	tgf-beta-four	0
<input type="checkbox"/>	L14	tgf-betafour	0
<input type="checkbox"/>	L15	tgfbetafour	0
<input type="checkbox"/>	L16	tgfbeta-four	0
<input type="checkbox"/>	L17	tgfb-four	0
<input type="checkbox"/>	L18	l8 or l10 or l11 or l12	34
<input type="checkbox"/>	L19	L18 not l1	27

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NCBI BLAST program reference [PMID:9254694]:  
Altschul S.F., Madden T.L., Schäffer A.A., Zhang J., Zhang Z., Miller W., Lipman D.J. Gapped BLAST and PSI-BLAST: a new generation of protein database search programs. Nucleic Acids Res. 25:3389-3402(1997).

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Query: 366 AA (of which 8% low-complexity regions filtered out)  
Date run: 2006-06-23 16:59:37 UTC+0100 on blast01.vital-it.ch  
Program: NCBI BLASTP 2.2.13 [Nov-27-2005]  
Database: UniProtKB  
3,203,912 sequences; 1,050,329,766 total letters  
UniProt Knowledgebase Release 8.1 consists of:  
UniProtKB/Swiss-Prot Release 50.1 of 13-Jun-2006: 223100 entries  
UniProtKB/TrEMBL Release 33.1 of 13-Jun-2006: 2965756 entries

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Db	AC	Description
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- |                          |    |        |  |
|--------------------------|----|--------|--|
| <input type="checkbox"/> | sp | O00292 | TGFB4_HUMAN Transforming growth factor beta-4 precursor. |
| <input type="checkbox"/> | tr | Q5TE89 | _HUMAN Left-right determination factor 2 [LEFTY2] [Homo  |



☐ tr Q53H67 \_HUMAN Left-right determination, factor B preproprotein  
☐ sp 075610 LEFTB\_HUMAN Left-right determination factor B precursor.  
☐ tr Q5TE94 \_HUMAN Left-right determination factor 1 [LEFTY1] [Homo  
☐ tr Q52M97 \_XENLA Hypothetical protein [Xenopus laevis (African cl  
☐ tr Q8BMF7 \_MOUSE 13 days embryo male testis cDNA, RIKEN full-leng  
☐ sp P57785 LEFTB\_MOUSE Left-right determination factor B precursor.  
☐ sp Q64280 TGFB4\_MOUSE Transforming growth factor beta-4 precursor.  
☐ tr Q3V2A9 \_MOUSE ES cells cDNA, RIKEN full-length enriched librar  
☐ tr Q5UCE3 \_RAT EBAF precursor [Rattus norvegicus (Rat)]  
☐ tr Q9DFC6 \_XENLA TGF-beta family member lefty-A [Xenopus laevis (  
☐ tr Q9DD36 \_XENLA Xantivin (Lefty-related factor Xatv) [Xantivin]  
☐ tr Q9DFC5 \_XENLA TGF-beta family member lefty-B [Xenopus laevis (  
☐ tr Q9PVN4 \_CHICK Lefty [Gallus gallus (Chicken)]  
☐ tr Q4SGU3 \_TETNG Chromosome 14 SCAF14590, whole genome shotgun se  
☐ tr Q9PW55 \_BRARE Antivin [lft1] [Brachydanio rerio (Zebrafish) (D  
☐ tr Q9W6I7 \_BRARE Signaling molecule lefty2 [lft2] [Brachydanio re  
☐ tr Q9PUK3 \_CHICK LEFTY-1 protein (Fragment) [LEFTY-1] [Gallus gal  
☐ tr Q9W6I6 \_BRARE Signaling molecule lefty1 (Lefty1) [lft1] [Brach  
☐ tr Q4H393 \_CIOIN Transforming growth factor beta superfamily sign  
☐ tr Q95YK6 \_CIOSA Lefty/antivin related protein [Cs-lfan] [Ciona s  
☐ tr Q6T265 \_PARLI Antivin/lefty [Paracentrotus lividus (Common sea  
☐ tr Q767A1 \_ORYLA Signaling molecule lefty1 (Fragment) [lefty1] [O  
☐ tr Q9XYQ7 \_LYTVA Bone morphogenetic protein BMP2/4 [BMP2/4] [Lyte  
☐ tr Q8JIJ4 \_9CICH Bmp4 protein [Bmp4] [Steatocranus casuarius (lio  
☐ tr Q8JIK1 \_9CICH Bmp4 protein [Bmp4] [Ctenochromis horei]  
☐ tr Q8JIJ9 \_HAPBU Bmp4 protein [Bmp4] [Haplochromis burtoni (Burto  
☐ tr Q8JIJ6 \_9CICH Bmp4 protein [Bmp4] [Labidochromis caeruleus (bl  
☐ tr Q8JFE2 \_BOUMI Bmp4 protein [Bmp4] [Boulengerochromis microlepi  
☐ tr Q78DH6 \_9CICH Bmp4 protein [Bmp4] [Gnathochromis permaxillaris  
☐ tr Q78DH5 \_9CICH Bmp4 protein [Bmp4] [Haplotaxodon microlepis]  
☐ tr Q78DH3 \_TANIR Bmp4 protein [Bmp4] [Tanganicodus irsacae (Spotf  
☐ tr Q8JIK2 \_ASTAL Bmp4 protein [Bmp4] [Astatoreochromis alluaudi (  
☐ tr Q8JIJ2 \_9CICH Bmp4 protein [Bmp4] [Tilapia rendalli (redbreast  
☐ tr Q78DH4 \_9CICH Bmp4 protein [Bmp4] [Ophthalmotilapia nasuta]  
☐ tr Q8JIJ7 \_9CICH Bmp4 protein [Bmp4] [Julidochromis transcriptus]  
☐ tr Q8JIJ3 \_9CICH Bmp4 protein [Bmp4] [Tropheus duboisi]  
☐ tr Q90YJ3 \_BRARE Anti-dorsalizing morphogenetic protein [admp] [B  
☐ sp P21275 BMP4\_MOUSE Bone morphogenetic protein 4 precursor (BMP.  
☐ tr Q8JIK0 \_9CICH Bmp4 protein [Bmp4] [Cyprichromis leptosoma]  
☐ tr Q8JIJ5 \_ORENI Bmp4 protein [Bmp4] [Oreochromis niloticus (Nile  
☐ tr Q3ULR1 \_MOUSE 5 days embryo whole body cDNA, RIKEN full-length  
☐ tr Q8UVQ2 \_BRARE Anti-dorsalizing morphogenetic protein [admp] [B

☐ tr Q8UVQ8 \_BRARE Anti-dorsalizing morphogenetic protein [admp] [B  
☐ tr Q8JIJ8 \_9CICH Bmp4 protein [Bmp4] [Haplochromis nyererei]  
☐ sp Q06826 BMP4\_RAT Bone morphogenetic protein 4 precursor (BMP-4.  
☐ tr Q6AYU9 \_RAT Bmp4 protein [Bmp4] [Rattus norvegicus (Rat)]  
☐ tr Q811S3 \_RAT Bone morphogenetic protein 4 [Bmp4] [Rattus norveg  
☐ tr Q8AYB5 \_ORYLA Bone morphogenetic protein 4 (Fragment) [Oryzias  
☐ tr Q91597 \_XENLA Anti-dorsalizing morphogenetic protein 1 precurs  
☐ sp Q90752 BMP4\_CHICK Bone morphogenetic protein 4 precursor (BMP.  
☐ tr O57574 \_BRARE Bone genetic protein 4 (Bone morphogenetic prote  
☐ tr P87380 \_BRARE Bone morphogenetic protein-4 (Fragment) [bmp4] [  
☐ tr Q28BW9 \_XENTR Novel protein similar to anti-dorsalizing morpho  
☐ tr Q6J3S5 \_PETMA Bone morphogenetic protein 24B [BMP24B] [Petromy  
☐ tr Q2KT33 \_ELECQ Bone morphogenetic protein 4 (Fragment) [Eleuthe  
☐ tr O13107 \_BRARE BMP4 [bmp4] [Brachydanio rerio (Zebrafish) (Dani  
☐ tr Q2KJH1 \_BOVIN Hypothetical protein [Bos taurus (Bovine)]  
☐ tr Q5I4I9 \_BOVIN Bone morphogenetic protein 4 (Fragment) [BMP4] [  
☐ tr Q8MJV5 \_SUNMU Bone morphogenetic protein 4 [sBmp4] [Suncus mur  
☐ tr Q1LWW7 \_BRARE Novel protein similar to bone morphogenetic prot  
☐ tr Q90YD6 \_XENTR Bone morphogenetic protein 4 (BMP4) [BMP-4] [Xen  
☐ tr Q2I6C6 \_CARPS Bone morphogenetic protein 4 (Fragment) [Bmp4] [  
☐ tr Q9MZV5 \_CANFA Bone morphogenetic protein 4 (Fragment) [bmp4] [  
☐ sp P12644 BMP4\_HUMAN Bone morphogenetic protein 4 precursor (BMP.  
☐ tr Q91703 \_XENLA Bone morphogenetic protein 4 [BMP-4] [Xenopus la  
☐ tr Q4SSG4 \_TETNG Chromosome undetermined SCAF14443, whole genome  
☐ tr Q6PAF3 \_XENLA LOC397874 protein [LOC397874] [Xenopus laevis (A  
☐ tr Q53XC5 \_HUMAN Full-length cDNA clone CS0DI018YL16 of Placenta  
☐ tr O73818 \_XENLA Bone morphogenetic protein 4 [BMP-4] [Xenopus la  
☐ tr Q6J3S6 \_PETMA Bone morphogenetic protein 24A [BMP24A] [Petromy  
☐ tr Q2VEW5 \_DIDAL Bone morphogenetic protein 4 [Didelphis albivent  
☐ sp P30885 BMP4\_XENLA Bone morphogenetic protein 4 precursor (BMP.  
☐ sp Q29607 BMP4\_DAMDA Bone morphogenetic protein 4 precursor (BMP.  
☐ tr Q90Y82 \_LAMJA LjBmp2/4a (Fragment) [LjBmp2/4a] [Lampetra japon  
☐ tr Q1PHR7 \_SACKO Bone morphogenetic protein 2/4 [Saccoglossus kow  
☐ tr Q2L6L2 \_MERUN Bone morphogenic protein-4 [BMP-4] [Meriones ung  
☐ tr Q9VQG9 \_DROME CG16987-PA, isoform A (Cg16987-pb, isoform b) (G  
☐ sp O08717 INHBE\_MOUSE Inhibin beta E chain precursor (Activin be.  
☐ tr Q91XH3 \_MOUSE Inhibin beta E [Inhbe] [Mus musculus (Mouse)]  
☐ tr Q9PVK1 \_CHICK Anti-dorsalizing morphogenetic protein [ADMP] [G  
☐ tr Q9PWR8 \_CARAU Activin beta B subunit precursor [Carassius aura  
☐ tr Q9W6T9 \_BRARE Activin beta B protein (Fragment) [inhbb] [Brach  
☐ tr Q4AEG6 \_RAT Bone morphogenetic protein 10 [Bmp10] [Rattus norv  
☐ tr Q27W10 \_9CNID BMP5-8 (Fragment) [Nematostella vectensis]

- ☐ tr Q589C7 \_MESAU Inhibin/activin beta B subunit (Fragment) [inhbb
- ☐ tr Q2LAG1 \_CTEID Activin beta B [Ctenopharyngodon idella (Grass c
- ☐ tr Q4SES4 \_TETNG Chromosome 3 SCAF14614, whole genome shotgun seq
- ☐ tr Q4VV68 \_BRARE Myostatin-II [gdf81] [Brachydanio rerio (Zebrafi
- ☐ sp O88959 INHBE\_RAT Inhibin beta E chain precursor (Activin beta.
- ☐ sp P17491 INHBB\_RAT Inhibin beta B chain precursor (Activin beta.
- ☐ sp Q04999 INHBB\_MOUSE Inhibin beta B chain precursor (Activin be.
- ☐ sp P27093 INHBB\_CHICK Inhibin beta B chain precursor (Activin be.
- ☐ tr Q3V1N0 \_MOUSE 15 days embryo head cDNA, RIKEN full-length enri
- ☐ tr Q1LYE4 \_BRARE Novel protein similar to vertebrate inhibin, alp
- ☐ tr Q90261 \_BRARE Activin beta B [inhbb] [Brachydanio rerio (Zebra
- ☐ sp P09529 INHBB\_HUMAN Inhibin beta B chain precursor (Activin be.
- ☐ tr Q53T31 \_HUMAN Hypothetical protein INHBB [INHBB] [Homo sapiens
- ☐ sp P58166 INHBE\_HUMAN Inhibin beta E chain precursor (Activin be.

### Graphical overview of the alignments

[Click here](#)

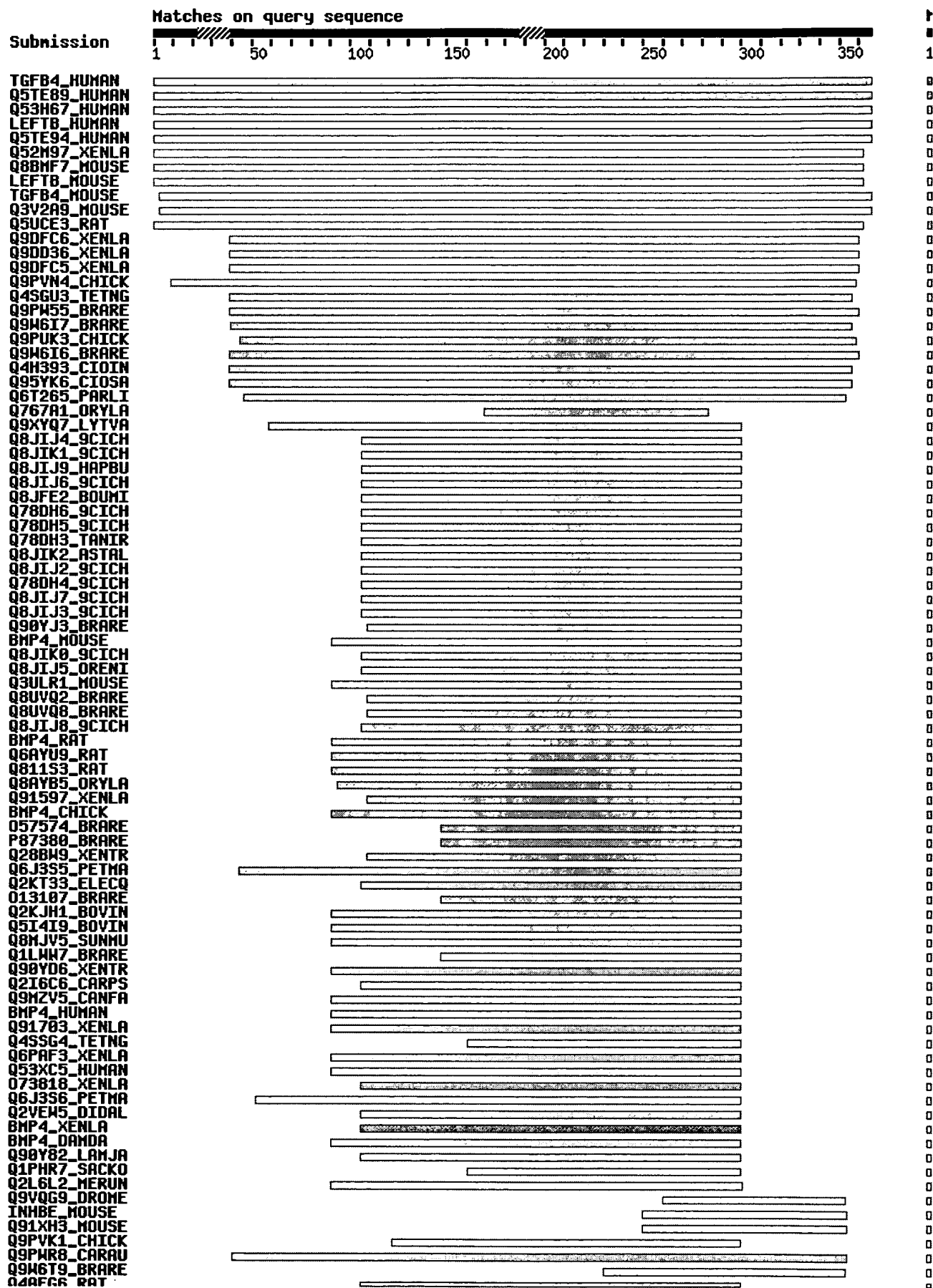
to resubmit your query after masking regions matching PROSITE profiles or Pfam HMMs

([?](#) Help) (use ScanProsite for more details about PROSITE matches)

#### Profile hits

#### Pfam hits





**Alignments**

sp     000292                   Transforming growth factor beta-4 precursor (TGF-  
          TGFB4\_HUMAN           beta-4)  
                                  (Endometrial bleeding-associated factor) (Left-  
                                  right  
                                  determination factor A) (Lefty-A protein) [EBAF]  
                                  [Homo  
                                  sapiens (Human)]

Score = 684 bits (1764), Expect = 0.0  
Identities = 337/366 (92%), Positives = 337/366 (92%)

Query: 1    MWPLWLCWALWVLPLAGPGAALTXXXXXXXXXXXXXXXXXXXXVPVLDRADMEKLVIPAH  
              MWPLWLCWALWVLPLAGPGAALT   VPVLDRADMEKLVIPAH  
Sbjct: 1    MWPLWLCWALWVLPLAGPGAALTEEQLLGSLLRQLQLSEVPVLDRADMEKLVIPAH

Query: 61   YVLLRRSHGDRSRGKRFSQSFREVAGRFLASEASTHLLVFGMEQRLPPNSELVQA  
             YVLLRRSHGDRSRGKRFSQSFREVAGRFLASEASTHLLVFGMEQRLPPNSELVQA  
Sbjct: 61   YVLLRRSHGDRSRGKRFSQSFREVAGRFLASEASTHLLVFGMEQRLPPNSELVQA

Query: 121   FQEPVPKAALHRHGRLSPRSAQARVTVEWLRVRDDGSNRTSLIDSRLVSVHESGWK  
             FQEPVPKAALHRHGRLSPRSAQARVTVEWLRVRDDGSNRTSLIDSRLVSVHESGWK  
Sbjct: 121   FQEPVPKAALHRHGRLSPRSAQARVTVEWLRVRDDGSNRTSLIDSRLVSVHESGWK

Query: 181   TEAVNFWXXXXXXXXXXXXXXXXXVSVQREHLGPLASGAHKLVRFASQGAPAGLGEPQLE  
             TEAVNFW   VSVQREHLGPLASGAHKLVRFASQGAPAGLGEPQLE  
Sbjct: 181   TEAVNFWQQLSRPRQPLLLQVSVQREHLGPLASGAHKLVRFASQGAPAGLGEPQLE

Query: 241   DLRDYGAQGDCDPEAPMTEGTRCCRQEMYIDLQGMKWAKNWWLEPPGFLAYECVGT  
             DLRDYGAQGDCDPEAPMTEGTRCCRQEMYIDLQGMKWAKNWWLEPPGFLAYECVGT  
Sbjct: 241   DLRDYGAQGDCDPEAPMTEGTRCCRQEMYIDLQGMKWAKNWWLEPPGFLAYECVGT

Query: 301   PEALAFNWPFLGPRQCIASETASLPMIVSIKEGGTRPQVVSLPNMRVQKCSCASD  
             PEALAFNWPFLGPRQCIASETASLPMIVSIKEGGTRPQVVSLPNMRVQKCSCASD  
Sbjct: 301   PEALAFNWPFLGPRQCIASETASLPMIVSIKEGGTRPQVVSLPNMRVQKCSCASD

Query: 361   PRRLQP 366  
             PRRLQP  
Sbjct: 361   PRRLQP 366

tr     Q5TE89                   Left-right determination factor 2 [LEFTY2] [Homo  
          Q5TE89\_HUMAN           sapiens (Human)]

Score = 684 bits (1764), Expect = 0.0

Identities = 337/366 (92%), Positives = 337/366 (92%)

```
Query: 1  MWPLWLCWALWVLPLAGPGAALTXXXXXXXXXXXXXXXXXXXXVPVLDRADMEKLVIPAH
          MWPLWLCWALWVLPLAGPGAALT                               VPVLDRADMEKLVIPAH
Sbjct: 1  MWPLWLCWALWVLPLAGPGAALTEEQLLGSLLRQLQLSEVPVLDRADMEKLVIPAH

Query: 61  YVLLRRSHGDRSRGKRFSQSFREVAGRFLASEASTHLLVFGMEQRLPPNSELVQA
          YVLLRRSHGDRSRGKRFSQSFREVAGRFLASEASTHLLVFGMEQRLPPNSELVQA
Sbjct: 61  YVLLRRSHGDRSRGKRFSQSFREVAGRFLASEASTHLLVFGMEQRLPPNSELVQA

Query: 121 FQEPVPKAALHRHGRLSPRSAQARVTVEWLRVRDDGSNRTSLIDSRLVSVHESGWK
          FQEPVPKAALHRHGRLSPRSAQARVTVEWLRVRDDGSNRTSLIDSRLVSVHESGWK
Sbjct: 121 FQEPVPKAALHRHGRLSPRSAQARVTVEWLRVRDDGSNRTSLIDSRLVSVHESGWK

Query: 181 TEAVNFWXXXXXXXXXXXXXXXXXVSVQREHLGPLASGAHKLVRFASQGAPAGLGEPQLE
          TEAVNFW                               VSVQREHLGPLASGAHKLVRFASQGAPAGLGEPQLE
Sbjct: 181 TEAVNFWQQLSRPRQPLLLQVSVQREHLGPLASGAHKLVRFASQGAPAGLGEPQLE

Query: 241 DLRDYGAQGDCDPEAPMTEGTRCCRQEMYIDLQGMKWAKNWWLEPPGFLAYECVGT
          DLRDYGAQGDCDPEAPMTEGTRCCRQEMYIDLQGMKWAKNWWLEPPGFLAYECVGT
Sbjct: 241 DLRDYGAQGDCDPEAPMTEGTRCCRQEMYIDLQGMKWAKNWWLEPPGFLAYECVGT

Query: 301 PEALAFNWPFLGPRQCIASETASLPMIVSIKEGGTRPQVVSLPNMRVQKCSCASD
          PEALAFNWPFLGPRQCIASETASLPMIVSIKEGGTRPQVVSLPNMRVQKCSCASD
Sbjct: 301 PEALAFNWPFLGPRQCIASETASLPMIVSIKEGGTRPQVVSLPNMRVQKCSCASD

Query: 361 PRRLQP 366
          PRRLQP
Sbjct: 361 PRRLQP 366
```

```
tr Q53H67      Left-right determination, factor B preproprotein variant
   Q53H67_HUMAN (Fragment)
                [LEFTY1] [Homo sapiens (Human)]
```

Score = 658 bits (1698), Expect = 0.0

Identities = 325/366 (88%), Positives = 329/366 (89%)

```
Query: 1  MWPLWLCWALWVLPLAGPGAALTXXXXXXXXXXXXXXXXXXXXVPVLDRADMEKLVIPAH
          M PLWLCWALWVLPLA PGAALT                               VP LDRADME+LVIP H
Sbjct: 1  MQPLWLCWALWVLPLASPGAALTGEQLLGSLLRQLQLKEVPTLDRADMEELVIPTH

Query: 61  YVLLRRSHGDRSRGKRFSQSFREVAGRFLASEASTHLLVFGMEQRLPPNSELVQA
          YV LL+RSHGDRSRGKRFSQSFREVAGRFLASEASTHLLVFGMEQRLPPNSELVQA
Sbjct: 61  YVALLQRSHGDRSRGKRFSQSFREVAGRFLASEASTHLLVFGMEQRLPPNSELVQA
```

Query: 121 FQEPVPKAALHRHGRLSPRSAQARVTVEWLRVRDDGSNRTSLIDSRLVSVHESGWK  
FQEPVPKAALHRHGRLSPRSAQARVTVEWLRVRDDGSNRTSLIDSRLVSVHESGWK  
Sbjct: 121 FQEPVPKAALHRHGRLSPRSAQARVTVEWLRVRDDGSNRTSLIDSRLVSVHESGWK

Query: 181 TEAVNFWXXXXXXXXXXXXXXXXXVSVQREHLGPLASGAHKLVRFASQGAPAGLGEPQLE  
TEAVNFW VSVQREHLGPLASGAHKLVRFASQGAPAGLGEPQLE  
Sbjct: 181 TEAVNFWQQLSRPRQPLLLQVSVQREHLGPLASGAHKLVRFASQGAPAGLGEPQLE

Query: 241 DLRDYGAQGDCDPEAPMTEGTRCCRQEMYIDLQGMKWAKNWVLEPPGFLAYECVGT  
DL DYGAQGDCDPEAPMTEGTRCCRQEMYIDLQGMKWA+NWVLEPPGFLAYECVGT  
Sbjct: 241 DLGDYGAQGDCDPEAPMTEGTRCCRQEMYIDLQGMKWAENWVLEPPGFLAYECVGT

Query: 301 PEALAFNWPFLGPRQCIASETASLPMIVSIKEGGRTRPQVVSLPNMRVQKCSCASD  
PEALAF WPFLGPRQCIASET SLPMIVSIKEGGRTRPQVVSLPNMRVQKCSCASD  
Sbjct: 301 PEALAFKWPFLGPRQCIASETDSLPMIVSIKEGGRTRPQVVSLPNMRVQKCSCASD

Query: 361 PRRLQP 366  
PRRLQP  
Sbjct: 361 PRRLQP 366

sp 075610 Left-right determination factor B precursor (Lefty-B  
LEFTB\_HUMAN protein)  
[LEFTB] [Homo sapiens (Human)]

Score = 654 bits (1688), Expect = 0.0  
Identities = 323/366 (88%), Positives = 328/366 (89%)

Query: 1 MWPLWLCWALWVLPLAGPGAALTXXXXXXXXXXXXXXXXXVPVLDRADMEKLVIPAH  
M PLWLCWALWVLPLA PGAALT VP LDRADME+LVIP H  
Sbjct: 1 MQPLWLCWALWVLPLASPGAALTGEQLLGSLLRQLQLKEVPTLDRADMEELVIPTH

Query: 61 YVLLRRSHGDRSRGKRFSQSFREVAGRFLASEASTHLLVFGMEQRLPPNSELVQA  
YV LL+RSHGDRSRGKRFSQSFREVAGRFLA EASTHLLVFGMEQRLPPNSELVQA  
Sbjct: 61 YVALLQRSHGDRSRGKRFSQSFREVAGRFLALEASTHLLVFGMEQRLPPNSELVQA

Query: 121 FQEPVPKAALHRHGRLSPRSAQARVTVEWLRVRDDGSNRTSLIDSRLVSVHESGWK  
FQEPVPKAALHRHGRLSPRSA+ARVTVEWLRVRDDGSNRTSLIDSRLVSVHESGWK  
Sbjct: 121 FQEPVPKAALHRHGRLSPRSARARVTVEWLRVRDDGSNRTSLIDSRLVSVHESGWK

Query: 181 TEAVNFWXXXXXXXXXXXXXXXXXVSVQREHLGPLASGAHKLVRFASQGAPAGLGEPQLE  
TEAVNFW VSVQREHLGPLASGAHKLVRFASQGAPAGLGEPQLE  
Sbjct: 181 TEAVNFWQQLSRPRQPLLLQVSVQREHLGPLASGAHKLVRFASQGAPAGLGEPQLE

Query: 241 DLRDYGAQGDCDPEAPMTEGTRCCRQEMYIDLQGMKWAKNWVLEPPGFLAYECVGT  
DL DYGAQGDCDPEAPMTEGTRCCRQEMYIDLQGMKWA+NWVLEPPGFLAYECVGT

Sbjct: 241 DLGDYGAQGDCDPEAPMTEGTRCCRQEMYIDLQGMKWAENWVLEPPGFLAYECVGT

Query: 301 PEALAFNWPFLGPRQCIASETASLPMIVSIKEGGRTRPQVVSLPNMRVQKSCASD  
PEALAF WPFLGPRQCIASET SLPMIVSIKEGGRTRPQVVSLPNMRVQKSCASD

Sbjct: 301 PEALAFKWPFLGPRQCIASETDSLPMIVSIKEGGRTRPQVVSLPNMRVQKSCASD

Query: 361 PRRLQP 366  
PRRLQP

Sbjct: 361 PRRLQP 366

tr Q5TE94 Left-right determination factor 1 [LEFTY1] [Homo  
Q5TE94\_HUMAN sapiens (Human)]

Score = 654 bits (1688), Expect = 0.0  
Identities = 323/366 (88%), Positives = 328/366 (89%)

Query: 1 MWPLWLCWALWVLPLAGPGAALTXXXXXXXXXXXXXXXXXXVPVLDRADMEKLVIPAH  
M PLWLCWALWVLPLA PGAALT VP LDRADME+LVIP H

Sbjct: 1 MQPLWLCWALWVLPLASPGAALTGEQLLGSLLRQLQLKEVPTLDRADMEELVIPTH

Query: 61 YVLLRRSHGDRSRGKRFSQSFREVAGRFLASEASTHLLVFGMEQRLPPNSELVQA  
YV LL+RSHGDRSRGKRFSQSFREVAGRFLA EASTHLLVFGMEQRLPPNSELVQA

Sbjct: 61 YVALLQRSHGDRSRGKRFSQSFREVAGRFLALEASTHLLVFGMEQRLPPNSELVQA

Query: 121 FQEPVPKAALHRHGRLSPRSAQARVTVEWLRVRDDGSNRTSLIDSRLVSVHESGWK  
FQEPVPKAALHRHGRLSPRSA+ARVTVEWLRVRDDGSNRTSLIDSRLVSVHESGWK

Sbjct: 121 FQEPVPKAALHRHGRLSPRSARARVTVEWLRVRDDGSNRTSLIDSRLVSVHESGWK

Query: 181 TEAVNFWXXXXXXXXXXXXXXXXXVSVQREHLGPLASGAHKLVRFASQGAPAGLGEPQLE  
TEAVNFW VSVQREHLGPLASGAHKLVRFASQGAPAGLGEPQLE

Sbjct: 181 TEAVNFWQQLSRPRQPLLLQVSVQREHLGPLASGAHKLVRFASQGAPAGLGEPQLE

Query: 241 DLRDYGAQGDCDPEAPMTEGTRCCRQEMYIDLQGMKWAENWVLEPPGFLAYECVGT  
DL DYGAQGDCDPEAPMTEGTRCCRQEMYIDLQGMKWA+NWVLEPPGFLAYECVGT

Sbjct: 241 DLGDYGAQGDCDPEAPMTEGTRCCRQEMYIDLQGMKWAENWVLEPPGFLAYECVGT

Query: 301 PEALAFNWPFLGPRQCIASETASLPMIVSIKEGGRTRPQVVSLPNMRVQKSCASD  
PEALAF WPFLGPRQCIASET SLPMIVSIKEGGRTRPQVVSLPNMRVQKSCASD

Sbjct: 301 PEALAFKWPFLGPRQCIASETDSLPMIVSIKEGGRTRPQVVSLPNMRVQKSCASD

Query: 361 PRRLQP 366  
PRRLQP

Sbjct: 361 PRRLQP 366



tr Q52M97 Hypothetical protein [Xenopus laevis (African  
Q52M97\_XENLA clawed frog)]

Score = 566 bits (1459), Expect = e-160

Identities = 274/364 (75%), Positives = 299/364 (82%), Gaps = 2/36

Query: 1 MWPLWLCWALWVLPLAGPGAALTXXXXXXXXXXXXXXXXXXXXVPVLDRADMEKLVIPAH  
M LWLCWALWVLPLAGPGAA+T P LD AD+E++ IP H  
Sbjct: 1 MKSLWLCWALWVLPLAGPGAAMTEEQVLSSLLQQLQLSQAPTLD SADVEEMAIPTH

Query: 61 YVLLRRSHGDRSRGKRFSQSFREVAGRFLASEASTHLLVFGMEQRLPPNSELVQA  
YV LL+ SH DRSRGKRFSQ+FREVAGRFL SE STHLLVFGMEQRLPPNSELVQA  
Sbjct: 61 YVALLQGSHADRSRGKRFSQNFREVAGRFLMSETSTHLLVFGMEQRLPPNSELVQA

Query: 121 FQEPVPKAALHRHGRLSPRSAQARVTVEWLRVRDDGSNRTSLIDSRLVSVHESGWK  
FQEPVP+ AL R RLSP SA+ARVT+EWLRVR+DGSNRT+LIDSRLVS+HESGWK  
Sbjct: 121 FQEPVVRTALRRFERLSPHSARARVTIEWLRVREDGSNRTALIDSRLVSIHESGWK

Query: 181 TEAVNFWXXXXXXXXXXXXXXXXXVSVQREHLGPLASGAHKLVRFAAQGAP--AGLGEPQ  
TEAVNFW VSVQREHLGP AHKLVRFA+QG P G GEPQ  
Sbjct: 181 TEAVNFWQQLSRPRQPLLLQVSVQREHLGPGTWSAHKLVRFAAQGTPDGKGQGEPO

Query: 239 TLDLRDYGAQGDCDPEAPMTEGTRCCRQEMYIDLQGMKWAKNWVLEPPGFLAYECV  
TLDL+DYGAQG+CDPE P+TEGTRCCRQEMY+DLQGMKWA+NW+LEPPGFL YECV  
Sbjct: 241 TLDLKDYGAGNCDPEVPVTEGTRCCRQEMYLDLQGMKWAENWILEPPGFLTYECV

Query: 299 QPPEALAFNWPFLGPRQCIASETASLPMIVSIKEGGRTRPQVVSLPNMRVQKCSA  
Q PE+L WPFLGPRQC+ASE SLPMIVS+KEGGRTRPQVVSLPNMRVQ CSA  
Sbjct: 301 QLPESLTIGWPFLGPRQCVASEMTSLPMIVSVKEGGRTRPQVVSLPNMRVQTCSCA

Query: 359 LVPR 362  
L+PR  
Sbjct: 361 LIPR 364

tr Q8BMF7 13 days embryo male testis cDNA, RIKEN full-length  
Q8BMF7\_MOUSE enriched  
library, clone:6030463A22 product:LEFT-RIGHT  
DETERMINATION FACTOR B (LEFTY-2 PROTEIN), full  
insert  
sequence (Left-right determination factor 2)  
[Lefty2]  
[Mus musculus (Mouse)]

Score = 566 bits (1459), Expect = e-160

Identities = 274/364 (75%), Positives = 299/364 (82%), Gaps = 2/36

Query: 1 MWPLWLCWALWVLPLAGPGAALTXXXXXXXXXXXXXXXXXXXXVPVLDRADMEKLVIPAH

```

      M  LWLCWALWVLPLAGPGAA+T                      P LD AD+E++ IP H
Sbjct: 1  MKSLWLCWALWVLPLAGPGAAMTEEQVLSSLLQQLQLSQAPTLD SADVEEMAIPTH

Query: 61  YVLLRRSHGDRSRGKRFSQSFREVAGRFLASEASTHLLVFGMEQRLPPNSELVQA
           YV LL+ SH DRSRGKRFSQ+ FREVAGRFL SE STHLLVFGMEQRLPPNSELVQA
Sbjct: 61  YVALLQGSHADRSRGKRFSQNFREVAGRFLMSETSTHLLVFGMEQRLPPNSELVQA

Query: 121 FQEPVPKAALHRHGRLSPRSAQARVTVEWLRVRDDGSNRTSLIDSRLVSVHESGWK
           FQEPVP+ AL R  RLSP SA+ARVT+EWLVRV+DGSNRT+LIDSRLVS+HESGWK
Sbjct: 121 FQEPVPRTALRRFERLSPHSARARVTIEWLRVREDGSNRTALIDSRLVSIHESGWK

Query: 181 TEAVNFWXXXXXXXXXXXXXXXXXVSVQREHLGPLASGAHKLVRFASQGAP--AGLGEPQ
           TEAVNFW                      VSVQREHLGP  AHKLVRFA+QG P  G GEPQ
Sbjct: 181 TEAVNFWQQLSRPRQPLLLQVSVQREHLGPGTWSAHKLVRFAAQGTPDGKGQGEPO

Query: 239 TLDLRDYGAQGDCEAPMTEGTRCCRQEMYIDLQGMKWAKNWWLEPPGFLAYECV
           TLDL+DYGAQG+CDPE P+TEGTRCCRQEMY+DLQGMKWA+NW+LEPPGFL YECV
Sbjct: 241 TLDLKDYGAGNCDPEVPVTEGTRCCRQEMYLDLQGMKWAENWILEPPGFLTYECV

Query: 299 QPPEALAFNWPFLGPRQCIASETASLPMIVSIKEGGRTRPQVVSLPNMRVQKCSA
           Q PE+L  WPFLGPRQC+ASE  SLPMIVS+KEGGRTRPQVVSLPNMRVQ  CSA
Sbjct: 301 QLPESLTIGWPFLGPRQCVASEMTSLPMIVSVKEGGRTRPQVVSLPNMRVQTCSCA

Query: 359 LVPR 362
           L+PR
Sbjct: 361 LIPR 364

```

```

sp      P57785          Left-right determination factor B precursor (Lefty-2
      LEFTB_MOUSE      protein)
                        [Leftb] [Mus musculus (Mouse)]

```

Score = 564 bits (1453), Expect = e-159  
 Identities = 273/364 (75%), Positives = 298/364 (81%), Gaps = 2/36

```

Query: 1  MWPLWLCWALWVLPLAGPGAALTXXXXXXXXXXXXXXXXXVPVLDRADMEKLVIPAH
           M  LWLCWALWVLPLAGPGAA+T                      P LD AD+E++ IP H
Sbjct: 1  MKSLWLCWALWVLPLAGPGAAMTEEQVLSSLLQQLQLSQAPTLD SADVEEMAIPTH

Query: 61  YVLLRRSHGDRSRGKRFSQSFREVAGRFLASEASTHLLVFGMEQRLPPNSELVQA
           YV LL+ SH DRSRGKRFSQ+ REVAGRFL SE STHLLVFGMEQRLPPNSELVQA
Sbjct: 61  YVALLQGSHADRSRGKRFSQNLREVAGRFLMSETSTHLLVFGMEQRLPPNSELVQA

Query: 121 FQEPVPKAALHRHGRLSPRSAQARVTVEWLRVRDDGSNRTSLIDSRLVSVHESGWK
           FQEPVP+ AL R  RLSP SA+ARVT+EWLVRV+DGSNRT+LIDSRLVS+HESGWK
Sbjct: 121 FQEPVPRTALRRFERLSPHSARARVTIEWLRVREDGSNRTALIDSRLVSIHESGWK

```

Query: 181 TEAVNFWXXXXXXXXXXXXXXXXXVSVQREHLGPLASGAHKLVRFA+QG P G GEPQ  
TEAVNFW VSVQREHLGP AHKLVRFA+QG P G GEPQ  
Sbjct: 181 TEAVNFWQQLSRPRQPLLLQVSVQREHLGPGTWSAHKLVRFAAQGTPDGKGQGEPO  
Query: 239 TLDLRDYGAQGDCDPEAPMTEGTRCCRQEMYIDLQGMKWAKNWNWLEPPGFLAYECV  
TLDL+DYGAQG+CDPE P+TEGTRCCRQEMY+DLQGMKWA+NW+LEPPGFL YECV  
Sbjct: 241 TLDLKDYGAQGNCDPEVPVTEGTRCCRQEMYLDLQGMKWAENWILEPPGFLTYECV  
Query: 299 QPPEALAFNWPFLGPRQCIASETASLPMIVSIKEGGRTRPQVVSLPNMRVQKCSA  
Q PE+L WPFLGPRQC+ASE SLPMIVS+KEGGRTRPQVVSLPNMRVQ CSA  
Sbjct: 301 QLPESLTIGWPFLGPRQCVASEMTSLPMIVSVKEGGRTRPQVVSLPNMRVQTCSCA  
Query: 359 LVPR 362  
L+PR  
Sbjct: 361 LIPR 364

sp Q64280 Transforming growth factor beta-4 precursor (TGF-  
TGFB4\_MOUSE beta-4) (Lefty  
protein) (Lefty-1 protein) (STRA3 protein) [Ebaf]  
[Mus  
musculus (Mouse)]

Score = 556 bits (1432), Expect = e-157

Identities = 271/365 (74%), Positives = 295/365 (80%), Gaps = 2/36

Query: 4 LWLCWALWVLPLAGPGAALTXXXXXXXXXXXXXXXXXVPVLDRADMEKLVIPAHVRA  
LWLCWALW L L ALT PVLD+AD+E +VIP+HVR  
Sbjct: 4 LWLCWALWALSLSLREALTGEQILGSLQLQQLQDQPPVLDKADVEGMVIPSHVRT  
Query: 64 LLRRSHGDRSRGKRFSQSFREVAGRFLASEASTHLLVFGMEQRLPPNSELVQAVLR  
LL+ SH RSRGKRFSQ+ REVAGRFL SE STHLLVFGMEQRLPPNSELVQAVLR  
Sbjct: 64 LLQHSASRSRGKRFSQNLREVAGRFLVSETSTHLLVFGMEQRLPPNSELVQAVLR  
Query: 124 PVPKAALHRHGRSLSPSAQARVTVEWLRVRDDGSNRTSLIDSRLVSVHESGWKAFF  
PVP+ AL R RLSP SA+ARVT+EWLR RDDGSNRT+LIDSRLVS+HESGWKAFF  
Sbjct: 124 PVPRTALRRQKRLSPHSARARVTIEWLRFRDDGSNRTALIDSRLVSIHESGWKAFF  
Query: 184 VNFVXXXXXXXXXXXXXXXXXVSVQREHLGPLASGAHKLVRFA+QG P G GEPQLEL  
VNFV VSVQREHLGP +HKLVRFA+QG P G GEPQLEL  
Sbjct: 184 VNFVQQLSRPRQPLLLQVSVQREHLGPGTWSSHKLVRFAAQGTPDGKGQGEPOLEL  
Query: 242 LRDYGAQGDCDPEAPMTEGTRCCRQEMYIDLQGMKWAKNWNWLEPPGFLAYECVGT  
L+DYGAQG+CDPEAP+TEGTRCCRQEMY+DLQGMKWA+NW+LEPPGFL YECVGT  
Sbjct: 244 LKDYGAQGNCDPEAPVTEGTRCCRQEMYLDLQGMKWAENWILEPPGFLTYECVGT

Query: 302 EALAFNWPFLGPRQCIASETASLPMIVSIKEGGRTRPQVVSLPNMRVQKCSCASDG  
E+L WPFLGPRQC+ASE SLPMIVS+KEGGRTRPQVVSLPNMRVQ CSCASDG  
Sbjct: 304 ESLTSRWPFLGPRQCVASEMTSLPMIVSVKEGGRTRPQVVSLPNMRVQTCSCASDG

Query: 362 RRLQP 366  
RRLQP  
Sbjct: 364 RRLQP 368

tr Q3V2A9 ES cells cDNA, RIKEN full-length enriched library,  
Q3V2A9\_MOUSE clone:2410018B15  
product:left-right determination, factor B, full insert  
sequence [Lefty1] [Mus musculus (Mouse)]

Score = 556 bits (1432), Expect = e-157  
Identities = 271/365 (74%), Positives = 295/365 (80%), Gaps = 2/36

Query: 4 LWLCWALWVLPLAGPGAALTXXXXXXXXXXXXXXXXXVPVLDRADMEKLVIPAHVRA  
LWLCWALW L L ALT PVLD+AD+E +VIP+HVR  
Sbjct: 4 LWLCWALWALSLSLREALTGEQILGSLQLQLDQPPVLDKADVEGMVIPSHVRT

Query: 64 LLRRSHGDRSRGKRFSQSFRVAGRFLASEASTHLLVFGMEQRLPPNSELVQAVLR  
LL+ SH RSRGKRFSQ+ REVAGRFL SE STHLLVFGMEQRLPPNSELVQAVLR  
Sbjct: 64 LLQSHASRSRGKRFSQNLREVAGRFLVSETSTHLLVFGMEQRLPPNSELVQAVLR

Query: 124 PVPKAALHRHGRLSPRSAQARVTVEWLRVRDDGSNRTSLIDSRLVSVHESGWKAFF  
PVP+ AL R RLSP SA+ARVT+EWLR RDDGSNRT+LIDSRLVS+HESGWKAFF  
Sbjct: 124 PVPRTALRRQKRLSPHSARARVTIEWLRFRDDGSNRTALIDSRLVSIHESGWKAFF

Query: 184 VNFWXXXXXXXXXXXXXVSVQREHLGPLASGAHKLVRFASQGAP--AGLGEPQLEL  
VNFW VSVQREHLGP +HKLVRF+QG P G GEPQLEL  
Sbjct: 184 VNFWQQLSRPRQPLLLQVSVQREHLGPGTWSSHKLVRF+AAQGTDPDGKGQGEQLEL

Query: 242 LRDYGAQGDCEAPMTEGTRCCRQEMYIDLQGMKWAKNWVLEPPGFLAYECVGTC  
L+DYGAQG+CDPEAP+TEGTRCCRQEMY+DLQGMKWA+NW+LEPPGFL YECVG+C  
Sbjct: 244 LKDYGAQGNCDPEAPVTEGTRCCRQEMYLDLQGMKWAENWILEPPGFLTYECVGSC

Query: 302 EALAFNWPFLGPRQCIASETASLPMIVSIKEGGRTRPQVVSLPNMRVQKCSCASDG  
E+L WPFLGPRQC+ASE SLPMIVS+KEGGRTRPQVVSLPNMRVQ CSCASDG  
Sbjct: 304 ESLTSRWPFLGPRQCVASEMTSLPMIVSVKEGGRTRPQVVSLPNMRVQTCSCASDG

Query: 362 RRLQP 366  
RRLQP  
Sbjct: 364 RRLQP 368

tr Q5UCE3 EBAF precursor [Rattus norvegicus (Rat)] 36  
Q5UCE3\_RAT al

Score = 553 bits (1425), Expect = e-156  
Identities = 267/362 (73%), Positives = 295/362 (81%)

Query: 1 MWPLWLCWALWVLPLAGPGAALTXXXXXXXXXXXXXXXXXVPVLDRADMEKLVIPAH  
M LWLCW L VLPLAGPGAA+T PVLDR D+E + IP H  
Sbjct: 1 MQSLWLCWTL CVLPLAGPGA AVTEEQVLSSLLKQLQLSQAPVLD RVDVEGMAIPTH

Query: 61 YVLLRRSHGDRSRGKRFSQSFREVAGRFLASEASTHLLVFGMEQRLPPNSELVQA  
YV LL+ SH DRSRGKRFSQ+FREVAGRFL SE S+HLLVFGMEQRLPPNSELVQA  
Sbjct: 61 YVALLQGSHADRSRGKRFSQNFREVAGRFLVSETSSHLLVFGMEQRLPPNSELVQA

Query: 121 FQEPVPKAALHRHGRLSPRSAQARVTVEWLRVRDDGSGNRTSLIDSRLVSVHESGWK  
FQEPVP+ AL R RL P SAQARVT+EWLVRV+DGSNRT+LIDSRLVS++ESGWK  
Sbjct: 121 FQEPVPRTALRRLERLPPHSAQARVTIEWLRVREDGSGNRTALIDSRLVSIYESGWK

Query: 181 TEAVNFWXXXXXXXXXXXXXXXXXVSVQREHLGPLASGAHKLVRFASQGAPAGLGEPQLE  
TEAVNFW VSVQREHLGP AHKLVRFA+QG P G GEPQLE  
Sbjct: 181 TEAVNFWQQLSRPRQPLLLQVSVQREHLGPGTWSAHKLVRFAAQGTPDGKGEPQLE

Query: 241 DLRDYGAQGD CDPEAPMTEGTRCCRQEMYIDLQGMKWAKNWVLEPPGFLAYECVGT  
DL+DYGAQG+CDPEAP+TEGTRCCR+EMY+DLQGMKWA+NW+LEPPGFL YECVG+  
Sbjct: 241 DLKDYGAQGNCDPEAPVTEGTRCCRKEMYLDLQGMKWAENWILEPPGFLIYECVGS

Query: 301 PEALAFNWPFLGPRQCIASETASLPMIVSIKEGGTRTPQVVSLPNMRVQKSCASD  
PE+L WPFLGPRQC+ASE SLPMIVSIKE G+TRPQVVSLPNMRVQ CSCASD  
Sbjct: 301 PESLTIGWPFLGPRQCVASEMTSLPMIVSIKEDGKTRPQVVSLPNMRVQTCSCASD

Query: 361 PR 362  
PR  
Sbjct: 361 PR 362

tr Q9DFC6 TGF-beta family member lefty-A [Xenopus laevis  
Q9DFC6\_XENLA (African clawed  
frog)]

Score = 231 bits (589), Expect = 3e-59  
Identities = 126/330 (38%), Positives = 193/330 (58%), Gaps = 16/3

Query: 40 VPVLDRADMEKLVIPAHVRAQYVLLRRSHGDRSRGK-----RFSQSFREVAG  
VP L++ D+E LVIP H++A+Y+ +L SH +R R R +++G  
Sbjct: 43 VPKLEKRDVENLVIPRHIQAKYMSMLH-SHRERKRRLPSLAGILRGISGNADISG

Query: 92 SEASTHLLVFGMEQRLPPNSELVQAVLRLRFQEPVPKAAALHRHGRLSPRSAQARVTV  
 S++S +VFGME R+P NSE+ A L+LF++P PK R + ARV+V  
 Sbjct: 102 SDSSKQTMVFGMESRIPENSEVTMAELKLFKKP-PKIMNVPERRFHRPVSNAARVSV

Query: 152 VRDDGSNRTSLIDSRLVSVHESGWKAFDVTEAVNFWXXXXXXXXXXXXXXXXXSVQREH  
 + DG+NRTSL+DSRLV + ESGW++FDVT+AV++W + V E  
 Sbjct: 161 ILKDGTNRTSLVDSRLVPIMESGWRSFDVTQAVHYW-MKSGGHSSMHLEIHVDGER

Query: 212 ASGAHKLVRFASQG-APAGLGEPQLELHTLDLRDYGAQGDCDPEAPMTEGTRCCRQ  
 AS K+VRF +Q + LG+P+L L TL+L ++GA+GDC + CCR+  
 Sbjct: 220 ASEMAKMVRFTTQSPSDNSLGKPELVLFNLDEHGARGDCSASGAKKDNI-CCRE

Query: 271 DLQGMKWAKNWWLEPPGFLAYECVGTCQQPPEALAFNWPFLGPRQCIASETASLPM  
 + + + W + W++EP G+ A+ C G+C+QP L+ ++ G R C E+A LP+  
 Sbjct: 279 NFRELTTWTQYWIIEPAGYNAFRGAGSCKQPKYPLSHHY---GERMCAVVESAPLPV

Query: 331 KEGGRTRPQVVSLPNMRVQKÇSCASD GALV 360  
 K+G T +V PNM V+KC C D +  
 Sbjct: 336 KKGDTYIEIEVAEFPNMIVEKÇGCTMDNIAI 365

tr Q9DD36 Xantivin (Lefty-related factor Xatv) [Xantivin]  
 Q9DD36\_XENLA [Xenopus laevis  
 (African clawed frog)]

Score = 228 bits (580), Expect = 3e-58

Identities = 128/337 (37%), Positives = 190/337 (56%), Gaps = 29/3

Query: 40 VPVLDRADMEKLVIPAHVRAQYVVLLRRSHGDRSRGKRFSQSFR-----EV  
 VP L++ D+E LVIP H++A+Y+ +L H R R KR S ++  
 Sbjct: 43 VPKLEKRDVENLVIPGHIQAKYMSML---HNHREKRRSLPSLAGILRGISGNADI

Query: 90 LASEASTHLLVFGMEQRLPPNSELVQAVLRLRFQEP-----VPKAAALHRHGRLSPRS  
 L S++S LVFGME R+P NSE+ A L+LF++P VP+ HR  
 Sbjct: 100 LYSDSSKQSLVFGMESRIPENSEVTMAELKLFKKPPKIMNVPERRFHRPVN-----

Query: 145 VTVEWLRVRDDGSNRTSLIDSRLVSVHESGWKAFDVTEAVNFWXXXXXXXXXXXXXXXXX  
 V+V ++ + DG+NRTSL+DSRLV + ESGW++FDVT+AV++W  
 Sbjct: 154 VSVYYVEILKDGTNRTSLVDSRLVPIMESGWRSFDVTQAVHYW-MRSGGQSSMHLE

Query: 205 REHLGPLASGAHKLVRFASQG-APAGLGEPQLELHTLDLRDYGAQGDCDPEAPMTE  
 E G AS K+VRF +Q + LG+P+L L TL+L + G +GDC +  
 Sbjct: 213 GERHGSHASEMAKMVRFTTQSPSDNSLGKPELVLFNLNEQGTRGDCSASGAKKD

Query: 264 CRQEMYIDLQGMKWAKNWWLEPPGFLAYECVGTCQQPPEALAFNWPFLGPRQCIAS  
 CR+E +I+ + + W + W++EP G+ A+ C G+C+QP L+ G R C

Sbjct: 272 CREEYFINFRELTWTQYWIIEPAGYNAFRCTGSCKQPKYPLSHY--HYGQRTCAVV

Query: 324 LPMIVSIKEGGRTRPQVVSLPNMRVQKCSCASDGALV 360

LP++ +K+G T +V PNM V+KC C D +

Sbjct: 330 LPVMYLVKKGDYTEIEVAEFPNMIVEKCGCTMDNIAI 366

tr Q9DFC5 TGF-beta family member lefty-B [*Xenopus laevis*  
Q9DFC5\_XENLA (African clawed  
frog)]

Score = 227 bits (579), Expect = 4e-58

Identities = 128/337 (37%), Positives = 190/337 (56%), Gaps = 29/3

Query: 40 VPVLDRADMEKLVIPAHVRAQYVVLLRRSHGDRSRGKRFSQSFR-----EV  
VP L++ D+E LVIP H++A+Y+ +L H R R KR S ++

Sbjct: 43 VPKLEKRDVENLVIPRHIQAKYMSML---HNRERKKRSLPSLAGILRGISGNADI

Query: 90 LASEASTHLLVFGMEQRLPPNSELVQAVLRLFQEP-----VPKAALHRHGRLSPRS  
L S++S LVFGME R+P NSE+ A L+LF++P VP+ HR

Sbjct: 100 LYSDSSKQSLVFGMESRIPENSEVTMAELKLFKKPPKIMNVPERRFHRPVN-----

Query: 145 VTVEWLRVRDDGSNRTSLIDSRLVSVHESGWKAFDVTEAVNFWXXXXXXXXXXXXX  
V+V ++ + DG+NRTSL+DSRLV + ESGW++FDVT+AV++W

Sbjct: 154 VSVYYVEILKDGTNRTSLVDSRLVPIMESGWRSFDVTQAVHYW-MRSGGQSSMHLE

Query: 205 REHLGPLASGAHKLVRFASQG-APAGLGEPQLELHTLDLRDYGAQGDCDPEAPMTE  
E G AS K+VRF +Q + LG+P+L L TL+L + G +GDC +

Sbjct: 213 GERHGSHASEMAKMVRFTTQSPSDNSLGKPELVLFNLNEQGTRGDCSASGAKKD

Query: 264 CRQEMYIDLQGMKWAKNWWLEPPGFLAYECVGTCQQPPEALAFNWPFLGPRQCIAS  
CR+E +I+ + + W + W++EP G+ A+ C G+C+QP L+ G R C

Sbjct: 272 CREEYFINFRELTWTQYWIIEPAGYNAFRCTGSCKQPKYPLSHY--HYGQRTCAVV

Query: 324 LPMIVSIKEGGRTRPQVVSLPNMRVQKCSCASDGALV 360

LP++ +K+G T +V PNM V+KC C D +

Sbjct: 330 LPVMYLVKKGDYTEIEVAEFPNMIVEKCGCTMDNIAI 366

tr Q9PVN4 Lefty [*Gallus gallus* (Chicken)] 362  
Q9PVN4\_CHICK ali

Score = 226 bits (575), Expect = 1e-57

Identities = 131/352 (37%), Positives = 187/352 (53%), Gaps = 8/35

Query: 10 LWVLPLAGPGAALTXXXXXXXXXXXXXXXXXXVPVLDRADMEKLVIPAHVRAQYVVLL  
 L+VL L A T VP L + D+ LVIP HV+ +Y+ +L  
 Sbjct: 9 LYVLCLVAMACFTQEGFKEVMLKQLGLSEVPKLHKRDLVDLVIPEHVKNKYISML

Query: 70 GDRSRGKRFSQSFRVAGR--FLASEASTHLLVFGMEQRLPPNSELVQAVLRLFQE  
 G R + + + G S+ +F ME R+P NSE+ A L+LF++  
 Sbjct: 69 GKRRASPSLASILQGIPGNAEVFYSDPMRQNFIFDMEGRIPKNSEVTMAELKLFKK

Query: 128 AALHRHGRLSPRSAQARVTVEWLRVRDDGSNRTSLIDSRLVSVHESGWKAFDVTEA  
 L P S ARV++ W++ + DG+NRTSLIDSRLV + ESGWK FDVT+A  
 Sbjct: 129 VNLPARQPHRPVS-NARVSIYWVQRQHDGTNRTSLIDSRLVPIRESGWKNFDVTQA

Query: 188 XXXXXXXXXXXXXVSVQREHLGPLASGAHKLVRFASQGA-PAGLGEPQLELHTLDL  
 V ++ E + A+ K VRF SQ A +G P+L L+TLDL  
 Sbjct: 188 -LRNKRQEPMVLQVWIEGERVASIAAEVAKSVRFTSQDAGDRAVGRPELVLYTLDL

Query: 247 AQGDCDPEAPMTEGTRCCRQEMYIDLQGMKWAKNWWLEPPGFLAYECVGTCQQPPE  
 GDC + T CCRQ+ YI+ + + W + WV+EP G+ AY C G C Q P  
 Sbjct: 247 GPGDCKDGVQAGKST-CCRQKHYNFRELSTQYWVIEPAGYQAYSCRGGCLQLPG

Query: 307 NWPFLGPRQCIASETASLPMIVSIKEGGRTRPQVVSLPNMRVQKCSASDGA 358  
 W R C +E++ LP++ ++ G T + PNM ++KCSC +DGA  
 Sbjct: 306 -WGG-RERACAVAESSPLPIMYLVRRGNHTEIEATEFPNMIIEKCSMADGA 355

tr Q4SGU3 Chromosome 14 SCAF14590, whole genome shotgun  
 Q4SGU3\_TETNG sequence  
 [GSTENG00018477001] [Tetraodon nigroviridis (Green  
 puffer)]

Score = 219 bits (559), Expect = 9e-56

Identities = 121/350 (34%), Positives = 189/350 (54%), Gaps = 42/3

Query: 40 VPVLDRADMEKLVIPAHVRAQYVVLLRRSHGDRSRGK-----RFSQSFRVAGR  
 +P + + D+E LV+PAH+R +Y+ +L+ H R R R +++G  
 Sbjct: 38 LPKIRKRDLENLVVPAHIRNKYLSMLKMHHSRRRSLPSLAGILRGIPGNADISGE

Query: 93 EASTHLLVFGMEQRLPPNSELVQAVLRLFQEPVPAALHRHGRLSPRSAQARVTVE  
 + + +VF ME R+P NSE+ A L+L+Q + + + ARV+V  
 Sbjct: 98 DTTRQRMVFDMEARIPDNSEVTMAELKLYQRASYQKRYAVEKKNHRPVSNAVSVY

Query: 153 RDDGSNRTSLIDSR-----LVSVHESGWKAFDVTEA  
 + DGSNRTSL+DSR L+ +HE+GWK+FDVT+A  
 Sbjct: 158 QRDGSNRTSLVDSRCVTSSDAIASASRPRSNLRLLVSHSLIPIHETGWKSFDVTQA

Query: 188 XXXXXXXXXXXXXVSVQREHLGPLASGAHKLVRFASQGA-PAG-LGEPQLELHTLDL



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      V ++ E G A+ K VRF +Q LG+P+L L+TLDL
Sbjct: 218 SKSGQKTPMHLE-VWIEGERPGSYAAEMAKSVRFTTQEQT DNTLGKPELILYTLDL

Query: 247 AQGDCDPEAPMTEGTRCCRQEMYIDLQGMKWAKNWWLEPPGFLAYECVGTCQQPPE
      + GDCD CCR++ +ID + + W + W++EP G+ A+ C GTC+QP
Sbjct: 277 SAGDCDVRSKDT---CCREQYFIDFRALTWTQYWIIEPAGYQAFRCAGTCKQPRR

Query: 307 NWPFLGPRQCIASETASLPMIVSIKEGGRTRPQVVSLPNMRVQKCSCASD 356
      G R+C+ SE+A LP++ +K+G T +V PNM V++C+CA D
Sbjct: 334 -----GERRCMVSESAPLPIMYLVKKG DYTEIEVAEFPNMIVERCACAMD 378

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tr Q9PW55 Antivin [lft1] [Brachydanio rerio (Zebrafish)]
   Q9PW55_BRARE (Danio rerio)]

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Score = 219 bits (558), Expect = 1e-55

Identities = 115/329 (34%), Positives = 185/329 (56%), Gaps = 18/3

```

Query: 40 VPVLDRADMEKLVIPAHVRAQYVVLLRRSHGDRSRGK-----RFSQSFREVAGR
      +P + + D+E LVIP HV+ +Y+ +L+ H + R R +++G
Sbjct: 39 IPQIHKRDLLENLVIPTHVKNKYISMLKLHHSRKRRLPSLAGILRGIPGNADISGE

Query: 93 EASTHLLVFGMEQRLPPNSELVQAVLRLFQEPVPKAALHRHGRLSPRSAQARVTVE
      + + +VF M R+P NSE+ A L+L+++ K ++ P + ARV++
Sbjct: 99 DTTRQRVVFEMTSRIPENSEVTMAELKLYKKAPHKRSIPERKGHHPVN-NARVSIY

Query: 153 RDDGSNRTSLIDSRLVSVHESGWKAFDVT EAVNFWXXXXXXXXXXXXXVSVQREHL
      + DGSNRTSL+DSRL+ +HE+GWK+FDVT+AV +W V ++ E
Sbjct: 158 QKDGSNRTSLVDSRLIPIHETGWKSFDVTQAVQYW-SRSRMEMPMHLEVWIEGERP

Query: 213 SGAHKLVRFASQGAPAG-LGEPQLELHTLDRDYGAQGDCEAPMTEGTRCCRQE
      + K V F +Q LG+P+L L+TL+L ++G+ GDC+ + CCR++
Sbjct: 217 AEMAKCVHFTTQDPDDNTLGKPELVLYTLNLEEFSSGDCENN---KDREMCCREQ

Query: 272 LQGMKWAKNWWLEPPGFLAYECVGTCQQPPEALAFNWPFLGPRQCIASETASLPMI
      + + W + W++EP G+ A+ C G C+QP + G R+C E+A LPM+
Sbjct: 274 FRALTWTQYWIIEPSGYQAFRCCKGGCRQPKRNYGY-----GERKCAVVESAPLPM

Query: 332 EGGRTTRPQVVSLPNMRVQKCSCASD GALV 360
      +G T +V PNM V+KC CA D V
Sbjct: 329 KGDYTEIEVAEFPNMIVEKCGCAMDNISV 357

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tr Q9W6I7 Signaling molecule lefty2 [lft2] [Brachydanio rerio]
   Q9W6I7_BRARE (Zebrafish)

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(Danio rerio)]

Score = 219 bits (557), Expect = 2e-55

Identities = 121/330 (36%), Positives = 183/330 (55%), Gaps = 25/3

Query: 41 PVLDRADMEKLVIPAHVRAQYVVLLRRSHGDRSRGK-----RFSQSFREVAGR  
 P + + D+E LV+PAH++++Y+ +L+ H R R R ++ G

Sbjct: 39 PRIQKRDLLENLVVPAHIKSKYLSMLKLHHQRRRRSLPSLAGILRGIHGNADITGEI

Query: 94 ASTHLLVFGMEQRLPPNSELVQAVLRLFQEPV--PKAALHRHGRLSPRSAQARVTV  
 + LVF ME RL N+E+ A L+LFQ P RH R ARV++

Sbjct: 99 TTRQRLVFDMEARLQENTTEVTMAELKLFQTAQAQSPSKPERRHHR---PINHARVSI

Query: 152 VRDDGSNRTSLIDSRLVSVHESGWKAFDVTEAVNFWXXXXXXXXXXXXXXXXXSVQREH  
 V ++GSNRTSL+DSRLV +HESGW++FDVT+A+++W V + E

Sbjct: 156 VLENGSNRTSLLDLSRLVPIHESGWRSFDVTQAIHYW-SKSQKKAPLHLEVWTEGER

Query: 212 ASGAHKLVRFASQGAPAG-----LGEPQLELHTLDLRDYGAQGDCDPEAPMTEGTR  
 A+ K VRFA+Q +G P+L L+TLDL +YG+QG+C+ ++

Sbjct: 215 AAEMAKRVRFATQDPKENTLEKDMGAPELVLYTLDLDEYGSQGCNCSS---PNSSK

Query: 267 EMYIDLQGMKWAKNWWLEPPGFLAYECVGTCQQPPEALAFNWPFLGPRQCIASETA  
 E +I+ + + W + W++EP G+ A+ C G C+QP + G R C E+A

Sbjct: 272 EHFINFRELTTWTQYWIIEPAGYQAFRCAGGCKQPKR----GFYGYGQRTCAVMESA

Query: 327 IVSIKEGGRTRPQVVSLPNMRVQKCSCASD 356  
 + +K+G T +V PNM V+KC C+ D

Sbjct: 328 MYLVKKGDYTEIEVAEFPNMIVEKCGCSMD 357

tr Q9PUK3 LEFTY-1 protein (Fragment) [LEFTY-1] [Gallus gallus  
 Q9PUK3\_CHICK (Chicken)]

Score = 219 bits (557), Expect = 2e-55

Identities = 122/317 (38%), Positives = 177/317 (55%), Gaps = 8/31

Query: 45 RADMEKLVIPAHVRAQYVVLLRRSHGDRSRGKRFSQSFREVAGR--FLASEASTHL  
 + D+ LVIP HV+ +Y+ +L+R G R + + + G S+

Sbjct: 2 KRDLVDLVIPEHVKNKYISMLKRHRGKRRASPSLASILQGIPGNAEVFYSDPMRQN

Query: 103 MEQRLPPNSELVQAVLRLFQEPVPAALHRHGRLSPRSAQARVTVIEWLRVRDDGSN  
 ME R+P NSE+ A L+LF++P+ + L P S ARV++ W++ + DG+N

Sbjct: 62 MEGRIPKNSEVTMAELKLFKKPLDRVNLPARQPHRPVS-NARVSIYWVQRQHDGTN

Query: 163 IDSRLVSVHESGWKAFDVTEAVNFWXXXXXXXXXXXXXXXXXSVQREHLGPLASGAHKL  
 IDSRLV + ESGWK FDVT+AV++W V ++ E + A+ K

Sbjct: 121 IDSRLVPIRESGWKNFDVTQAVHYW-LRNKRQEPMLVQVWIEGERVASIAAEVAKS

Query: 223 SQGA-PAGLGEPQLELHTLDRDYGAQGDCDPEAPMTEGTRCCRQEMYIDLQGMKW  
 SQ A +G P+L L+TLDL DYG GDC + T CCRQ+ YI+ + + W

Sbjct: 180 SQDAGDRAVGRPELVLYTLDELDYGGPGDCKDGVQAGKST-CCRQKHYINFRELSW

Query: 282 VLEPPGFLAYECVGTCQQPPEALAFNWPFLGPRQCIASETASLPMIVSIKEGGRT  
 V+EP G+ AY C G C Q P L W R C +E++ LP++ ++ G T

Sbjct: 239 VIEPAGYQAYSCRGGCLQLPGPLQL-WGG-RERACAVAESSPLPIMYLVRRGNHTE

Query: 342 SLPNMRVQKCSCASDGA 358  
 PNM ++KCSC +DGA

Sbjct: 297 EFPNMIIEKCSCMADGA 313

tr Q9W6I6 Signaling molecule lefty1 (Lefty1) [lft1]  
 Q9W6I6\_BRARE [Brachydanio rerio  
 (Zebrafish) (Danio rerio)]

Score = 216 bits (551), Expect = 8e-55

Identities = 114/329 (34%), Positives = 185/329 (56%), Gaps = 18/3

Query: 40 VPVLDRADMEKLVIPAHVRAQYVLLRRSHGDRSRGK-----RFSQSFREVAGR  
 +P + + D+E LVIP +V+ +Y+ +L+ H + R R +++G

Sbjct: 39 IPQIHKRDLENLVIPTNVKNKYISMLKLHHSRKRRSLPSLAGILRGIPGNADISGE

Query: 93 EASTHLLVFGMEQRLPPNSELVQAVLRLFQEPVPKAAALHRHGRLSPRSAQARVTVE  
 + + +VF M R+P NSE+ A L+L+++ K ++ P + ARV++

Sbjct: 99 DTTRQRVVFEMTSRIPENSEVTMAELKLYKKAPHKRSIPERKGHHPVN-NARVSIY

Query: 153 RDDGSNRTSLIDSRLSVHESGWKAFDVTEAVNFWXXXXXXXXXXXXXSVSVQREHL  
 + DGSNRTSL+DSRL+ +HE+GWK+FDVT+AV +W V ++ E

Sbjct: 158 QKDGSNRTSLVDSRLIPIHETGWKSFDVTQAVQYW-SRSRMEMPMHLEVWIEGERP

Query: 213 SGAHKLVRFASQGAPAG-LGEPQLELHTLDRDYGAQGDCDPEAPMTEGTRCCRQE  
 + K V F +Q LG+P+L L+TL+L ++G+ GDC+ + CCR++

Sbjct: 217 AEMAKCVHFTTQDPDDNTLGKPELVLYTLNLEEFSSGDCENN---KDREMCCREQ

Query: 272 LQGMKWAKNWWLEPPGFLAYECVGTCQQPPEALAFNWPFLGPRQCIASETASLPMI  
 + + W + W++EP G+ A+ C G C+QP + G R+C E+A LPM+

Sbjct: 274 FRALTWTQYWIIEPSGYQAFRCKGGCRQPKRNYGY-----GERKCAVVESAPLPM

Query: 332 EGGRTRPQVVSLPNMRVQKCSCASDGA 360  
 +G T +V PNM V+KC CA D V

Sbjct: 329 KGDYTEIEVAEFPNMIVEKCGCAMDNISV 357

tr Q4H393 Transforming growth factor beta superfamily  
 Q4H393\_CIOIN signaling ligand  
 [Ci-lefty/antivin] [Ciona intestinalis]

Score = 152 bits (385), Expect = 1e-35

Identities = 105/356 (29%), Positives = 165/356 (46%), Gaps = 51/3

Query: 40 VPVLDRADMEKLVIPAHVRAQYVVVL-----LRRSHGDRSRGKRFSQS-FREV---  
 +P + D+ ++V+P H+RA+Y L L R+ RS G + FR V  
 Sbjct: 37 LPTFTQMDLSQVVVPDHIRARYEQLVAARESRLGRNRRIRSAGPSLAGLFRNVHQK

Query: 87 GRFLASEASTHLLVFGMEQRLPPNSELVQAVLRLFQEPVPKAAALHRHGRLSP----  
 G + S+ L F ME ++P + + A LRLF++ L H RL  
 Sbjct: 97 GDVIYSDTFREQLKFDMEGKIPDKTTITMAELRLFKK-----LPNHSRLGAYTVK

Query: 139 -----RSAQ----ARVTVEWLRVRDDGSNRTSLIDSRLVSVHESGWKA  
 RS Q ARV++ +G T L+DSRL+ V+ SGW++  
 Sbjct: 151 SGRNDVERPSVRRSPQVIRHARVSIHHSPLPLNGDVITELVDSRLIMVNGSGWQS

Query: 182 EAVNFWXXXXXXXXXXXXXXXXXSVQREHLGPLASGAHKLVRFASQG-APAGLGEPQLE  
 A+ W + VQ G +AS +++RF Q A P+L  
 Sbjct: 211 SAIRKWQRHPVKFMTITLELKVQSTRPGRVASEVARMIRFTGQKVALDSPRRPELV

Query: 241 DLRDYGAQGDCDPEAPMTEGTRCCRQEMYIDLQGMKWAKNWVLEPPGFLAYECVGT  
 + + DC +CCR++ +I + M+WAK+W++EP G+ AY+C G  
 Sbjct: 271 E-EEKTRTNDCSASRHRRH-RKCCREKRFISFREMEWAKDWIIEPSGYDAYQCAGG

Query: 301 PEALAFNWPFLGPRQCIASETASLPMIVSIKEGGRTRPQVVSLLPNMRVQKSCASD  
 + PR C +E+ SLP++ +K+G T+ +V PNM V+KC+C+ D  
 Sbjct: 329 RRKNSKR----SPRSCTVAESTSLPVMYLVKGDGDKVEVSEFPNMVVEKACASLD

tr Q95YK6 Lefty/antivin related protein [Cs-lfan] [Ciona  
 Q95YK6\_CIOSA savignyi]

Score = 145 bits (365), Expect = 3e-33

Identities = 107/348 (30%), Positives = 160/348 (45%), Gaps = 43/3

Query: 40 VPVLDRADMEKLVIPAHVRAQYVVLLRR-SHGDRSRGKRFSQS-FREV-----AG  
 VP ++ +VIP R +Y ++ + + +R+R Q FR V G  
 Sbjct: 32 VPRFTHNEVRNVVIPDETTRRKYERMVEKMTKLERNRRSSSLQDLFRSVHKKTGIEG

Query: 92 SEASTHLLVFGMEQRLPPNSELVQAVLRLFQEPVPKAAALHRHGRL-----  
 S+ L F ME RLP + + A LRLF++ L H R+  
 Sbjct: 92 SDTFREELKFDMEGRLPDDYMISMAELRLFKK-----LPNHNRIISRLRTPSGNR

Query: 137 --SPRSAQ-----ARVTVEWLRVRDDGSNRTSLIDSRLVSVHESGWKAFDVT EAVN  
                   S R Q       ARV++           DG    T L+DSRL+ V+ SGW   FDVT A+  
 Sbjct: 146 LSSARGRQQVIRNARVSIHLSLPLPDGGAVTELVD SRLILVNGSGWHTFDV TSAIR

Query: 190 XXXXXXXXXXXXSVQREHLGPLASGAHKLVRFASQG-APAGLGEPQLELHTLDLRD  
                           + VQ       G A+    +L+RF   Q A       P+L ++T + ++  
 Sbjct: 206 HPVRYMTITLELKVQSSSPGRAAAELARLIRFTGQRVALDSPRRPELVVYT-NAKE

Query: 249 GDCDPEAPMTEGTRCCRQEMYIDLQGMKWAKNWWLEPPGFLAYECVGTCQQPPEAL  
                   DC           + +CCR+   +++ +   KW+K+W+LEP GF AY C G C+  
 Sbjct: 265 SDCSSSRHNRQH-KCCRENRFVNFRET KWSKH WILEPAGFNAYHCAGGCRSDRRRN

Query: 309 PFLGPRQCIASETASLPMIVSIKEGGRT RPQVVSLPNMRVQKCSCASD 356  
                   PR C A+ET SLP++ +K+GG    +V    PNM ++KCSA D  
 Sbjct: 323 ---APRSCSATETNSLPIMYLVKKGAIHVEVSEFPNMVIEKCSCALD 367

tr    Q6T265                           **Antivin/lefty [Paracentrotus lividus (Common sea urchin)]**  
       Q6T265\_PARLI

Score = 101 bits (252), Expect = 4e-20

Identities = 89/359 (24%), Positives = 138/359 (38%), Gaps = 60/35

Query: 47 DMEKLVIPAHVRAQYVVLLRRSHGDRSRGKRFSQSFREVAGRFLASEASTHLLVFG  
                   D   L +P H+R QY   + R+       R+    +       E+ G    +E + L F  
 Sbjct: 52 DASTLTVPDHLRFQYESMHRQHRVRRAYITKGIHKNEEIYGEVSYTERNRQLFTFD

Query: 107 LPPNSELVQAVLRLFQE-----PVPKAALHRHGRLSPRSAQARVT--  
                   +P   SE++ A L+++E                           P + H H    + S + V  
 Sbjct: 111 IPEGSEVIMAECLKVYKERPNHSIFKPEGEEGEAPHSNNHDHVHSALVSIKQLVDQE

Query: 147 VEWLRVRDDGSNR-----TSLIDSRLVSVHESGWKAFDVT EAVNFWXXXXXXXXXX  
                   E   + D+ N+       T ID R +++ +GWK FDVT   + W  
 Sbjct: 171 AEPADLADEVVNQHDGMDTITIDQREMTLKGAGWKVFDVTNTIQTWVADSDSNLGV

Query: 202 SVQREHLGPLASGAHKL-----VRFASQGAPAGLGEPQLELHTLDLRDYGAQGDCD  
                   H+ P+ G H           + FA+   P    P       +    A    +  
 Sbjct: 229 -----HIDPIEGGHHAQQVVDEMVFATDFFPETPDSPDSRPVLVIYTTKYAPASDE

Query: 257 MTEGT---RCCRQEMYIDLQGMKWAKNWWLEPPGFLAYECVGTCQQPPEAL---AF  
                   EG       RCCR+ Y+D + + W    W++EP GF A++C G C P       F  
 Sbjct: 284 RYEGEEHRCRRRK YVDFRDL SWT SRWII EPAGFEAFDCYGPCHNPRSRHIRDVF

Query: 311 LGP-----RQCIASETASLPMI-VSIKEGGRT RPQVVSLPNMRVQK  
                   G                           R C S ++SLPM+ +S    G    +V +PNM V+  
 Sbjct: 344 FGASSSGSSIFGAGSGGHRTCGVSRSSSLPMMYLSETPSGTVELKVEEIPNMIVED

tr Q767A1 Signaling molecule lefty1 (Fragment) [lefty1]  
Q767A1\_ORYLA [Oryzias latipes  
(Medaka fish) (Japanese ricefish)]

Score = 83.2 bits (204), Expect = 1e-14

Identities = 41/115 (35%), Positives = 66/115 (57%), Gaps = 5/115

Query: 170 VHESGWKAFDVT EAVNFWXXXXXXXXXXXXXXXXXVSVQREHLGPLASGAHKLVRFASQG  
+HE+GWK+FDVT+AV++W V ++ E G A+ K VRF +Q  
Sbjct: 2 IHETGWKSFDVTQAVHYW-SKTQQKTPMHLEVWIEGERPGSYAAEVAKSVRFTTQE  
  
Query: 230 L-GEPQLELHTLDLRDYGAQGDCDPEAPMTEGTRCCRQEMYIDLQGMKWAKNWWL  
G+P+L L+TL+L +YG++GDCD CCR++ +ID + + W + W++  
Sbjct: 61 TSGKPELVLYTLNLEEYGSRGDCD---VYQSKDTCCREQYFIDFRALTWTQYWII

tr Q9XYQ7 Bone morphogenetic protein BMP2/4 [BMP2/4]  
Q9XYQ7\_LYTVA [Lytechinus variegatus  
(Sea urchin)]

Score = 69.7 bits (169), Expect = 2e-10

Identities = 70/280 (25%), Positives = 110/280 (39%), Gaps = 47/28

Query: 60 QYVLLRRSHGDRSRGKRFSQSF-----REVAGRFLASEASTHLLV  
QY++ L RSH + G F E AG+ L +E H ++  
Sbjct: 81 QYMDLYRSHTHQDGISMHFDFDHLSTGTANTIRSYHHEDAGQVLPTEHHRHTVI  
  
Query: 105 QRLPPNSELVQAVLRLFQEPVPKAAALHRHGRLSPRSA-----QARVTVEWLRVRD  
+P L A LRLF++ + + ++ + L R + R+ V + ++  
Sbjct: 141 T-MPAEEVLTM AELRLFRKDLEEHSAKRHALDDRKSLEPIHYMQRINVFHI-LKP  
  
Query: 159 RTS---LIDSRLVSVHESGWKAFDVT EAVNFWXXXXXXXXXXXXXXXXXVSVQREHLGPL  
R + LID+RLV V S W++FDV AV W + R P  
Sbjct: 199 RDTIKRLIDTRLVDVRNSSWESFDVRPAVTSWVEVPEKNHGLEIELIDSRGRPSP-  
  
Query: 216 HKLVRFASQGAPAGLGEPQLELHTL-----DLRDYGAQGDCDPEAPMTEGTR---  
H VR + P+ + E Q E + Y G +P + G +  
Sbjct: 255 HHHVRVTREADPSKVQELQNEEDERWFQTRPQIVTYSDDGR-TKRSPSSRGRKRKG  
  
Query: 263 --CCRQEMYIDLQGMKWAKNWWLEPPGFLAYECVGTCQQP 300  
C R +Y+D + W +W++ P G+ AY C G C P  
Sbjct: 314 ANCRRHPLYVDFSDVHW-NDWIVAPAGYQAYYCHGECPPF 352

tr Q8JIJ4 Bmp4 protein [Bmp4] [Steatocranus casuarius  
Q8JIJ4\_9CICH (lionhead cichlid)]

Score = 67.4 bits (163), Expect = 8e-10

Identities = 61/207 (29%), Positives = 91/207 (43%), Gaps = 25/207

Query: 107 LPPNSELVQAVLRLFQEPVPKAALHRHGRLSPRSAQARVTV-EWLRVRDDGSNRTS  
+P + L A LRL++ + +A +S A R+ V E L+ G T  
Sbjct: 145 IPEDELLSSAELRLYRHQIDEAIADA---ISDDQALHRINVYEVLKAPRPGQLITQ

Query: 166 RLVS VHESGWKAFDVTEAVNFWXXXXXXXXXXXXXXXXXVSVQREHLG--PLASGAHKLV  
RLV + S W++FDV+ AV W ++V+ HL P G H +  
Sbjct: 202 RLVRHNASRWESFDVSPAVLRW----TRERLPNYGLAVEVLHLNQTPRHQGRHVRI

Query: 224 QGAPAGLGEPQLELHTLDLRDYGAQGDCDP-----EAPMTEGTR----CCRQEMY  
P GE +L L L +G G P +P G + C R +Y  
Sbjct: 258 HQEP---GEDWEQLRPL-LVTFGHDGKGHPLTRRTKRSPRQRGRKRNRCRRHALY

Query: 274 GMKWAKNWVLEPPGFLAYECVGTCQQP 300  
+ W +W++ PPG+ AY C G C P  
Sbjct: 314 DVGW-NDWIVAPPGYQAYYCHGECPPF 339

tr Q8JIK1 Bmp4 protein [Bmp4] [Ctenochromis horei] 40  
Q8JIK1\_9CICH a.

Score = 66.6 bits (161), Expect = 1e-09

Identities = 60/207 (28%), Positives = 91/207 (43%), Gaps = 25/207

Query: 107 LPPNSELVQAVLRLFQEPVPKAALHRHGRLSPRSAQARVTV-EWLRVRDDGSNRTS  
+P + L A LRL++ + +A +S A R+ V E L+ G T  
Sbjct: 145 IPEDELLSSAELRLYRHQIDEAIADA---ISDDQALHRINVYEVLKAPRPGQLITQ

Query: 166 RLVS VHESGWKAFDVTEAVNFWXXXXXXXXXXXXXXXXXVSVQREHLG--PLASGAHKLV  
RLV + S W++FDV+ AV W ++V+ HL P G H +  
Sbjct: 202 RLVRHNASRWESFDVSPAVLRW----TRERLPNYGLAVEVLHLNQTPRHQGRHVRI

Query: 224 QGAPAGLGEPQLELHTLDLRDYGAQGDCDP-----EAPMTEGTR----CCRQEMY  
P GE +L L L +G G P +P G + C R +Y  
Sbjct: 258 HQEP---GEDWKQLRPL-LVTFGHDGKGHPLTRRTKRSPRQRGRKRNRCRRHALY

Query: 274 GMKWAKNWVLEPPGFLAYECVGTCQQP 300  
+ W +W++ PPG+ AY C G C P  
Sbjct: 314 DVGW-NDWIVAPPGYQAYYCHGECPPF 339

tr Q8JIJ9            **Bmp4 protein [Bmp4] [Haplochromis burtoni (Burton's**  
Q8JIJ9\_HAPBU **mouthbrooder)]**

Score = 66.2 bits (160), Expect = 2e-09

Identities = 60/207 (28%), Positives = 91/207 (43%), Gaps = 25/207

Query: 107 LPPNSELVQAVLRLRFQEPVPKAAALHRHGRLSPRSAQARVTV-EWLRVRDDGSNRTS  
+P + L A LRL++ + +A +S A R+ V E L+ G T  
Sbjct: 145 IPEDELLSSAELRLYRHQIDEAIADA---ISDDQALHRINVYEVLKAPRPGQLITQ  
  
Query: 166 RLVSVHESGWKAFDVTEAVNFWXXXXXXXXXXXXXXXXXVSVQREHLG--PLASGAHKLV  
RLV + S W++FDV+ AV W ++V+ HL P G H +  
Sbjct: 202 RLVRHNASRWESFDVSPAVLRW----TRERLPNYGLAVEVLHLNQTTPRHQGRHVRI  
  
Query: 224 QGAPAGLGEPQLELHTLDLRDYGAQGDCDP-----EAPMTEGTR----CCRQEMY  
P GE +L L L +G G P +P G + C R +Y  
Sbjct: 258 HQEP---GEDWEQLRPL-LVTFGHDGKGHPLTRRTKRSRQGRKRNRNCRHALY  
  
Query: 274 GMKWAKNWWLEPPGFLAYECVGTCQQP 300  
+ W +W++ PPG+ AY C G C P  
Sbjct: 314 DVGW-NDWIVAPPGYQAYYCHGECFPF 339

tr Q8JIJ6            **Bmp4 protein [Bmp4] [Labidochromis caeruleus (blue**  
Q8JIJ6\_9CICH **streak hap)]**

Score = 66.2 bits (160), Expect = 2e-09

Identities = 60/207 (28%), Positives = 91/207 (43%), Gaps = 25/207

Query: 107 LPPNSELVQAVLRLRFQEPVPKAAALHRHGRLSPRSAQARVTV-EWLRVRDDGSNRTS  
+P + L A LRL++ + +A +S A R+ V E L+ G T  
Sbjct: 145 IPEDELLSSAELRLYRHQIDEAIADA---ISDDQALHRINVYEVLKAPRPGQLITQ  
  
Query: 166 RLVSVHESGWKAFDVTEAVNFWXXXXXXXXXXXXXXXXXVSVQREHLG--PLASGAHKLV  
RLV + S W++FDV+ AV W ++V+ HL P G H +  
Sbjct: 202 RLVRHNASRWESFDVSPAVLRW----ARERLPNYGLAVEVLHLNQTTPRHQGRHVRI  
  
Query: 224 QGAPAGLGEPQLELHTLDLRDYGAQGDCDP-----EAPMTEGTR----CCRQEMY  
P GE +L L L +G G P +P G + C R +Y  
Sbjct: 258 HQEP---GEDWEQLRPL-LVTFGHDGKGHPLTRRTKRSRQGRKRNRNCRHALY  
  
Query: 274 GMKWAKNWWLEPPGFLAYECVGTCQQP 300  
+ W +W++ PPG+ AY C G C P  
Sbjct: 314 DVGW-NDWIVAPPGYQAYYCHGECFPF 339



tr Q8JFE2 Bmp4 protein [Bmp4] [Boulengerochromis microlepis (Giant  
Q8JFE2\_BOUMI cichlid)]

Score = 66.2 bits (160), Expect = 2e-09

Identities = 60/207 (28%), Positives = 91/207 (43%), Gaps = 25/207

Query: 107 LPPNSELVQAVLRLRFQEPVPKAAALHRHGRLSPRSAQARVTV-EWLRVRDDGSNRTS  
+P + L A LRL++ + +A +S A R+ V E L+ G T

Sbjct: 145 IPEDELLSSAELRLYRHQIDEAIADA---ISDDQALHRINVYEVLKAPRPGQLITQ

Query: 166 RLVS VHESGWKAFDVTEAVNFWXXXXXXXXXXXXXXXXXVSVQREHLG--PLASGAHKLV  
RLV + S W++FDV+ AV W ++V+ HL P G H +

Sbjct: 202 RLVRHNASRWESFDVSPAVLRW----TRERLPNYGLAVEVLHLNQTTPRHQGRHVRI

Query: 224 QGAPAGLGEPQLELHTLDRDYGAQGDCDP-----EAPMTEGTR----CCRQEMY  
P GE +L L L +G G P +P G + C R +Y

Sbjct: 258 HQEP---GEDWEQLRPL-LVTFGHDGKGHPLTRRTKRSPRQRGRKRNRCRRHALY

Query: 274 GMKWAKNWWLEPPGFLAYECVGTCQQP 300

+ W +W++ PPG+ AY C G C P

Sbjct: 314 DVGW-NDWIVAPPGYQAYYCHGECFPF 339

tr Q78DH6 Bmp4 protein [Bmp4] [Gnathochromis permaxillaris] 4  
Q78DH6\_9CICH 6

Score = 66.2 bits (160), Expect = 2e-09

Identities = 60/207 (28%), Positives = 91/207 (43%), Gaps = 25/207

Query: 107 LPPNSELVQAVLRLRFQEPVPKAAALHRHGRLSPRSAQARVTV-EWLRVRDDGSNRTS  
+P + L A LRL++ + +A +S A R+ V E L+ G T

Sbjct: 145 IPEDELLSSAELRLYRHQIDEAIADA---ISDDQALHRINVYEVLKAPRPGQLITQ

Query: 166 RLVS VHESGWKAFDVTEAVNFWXXXXXXXXXXXXXXXXXVSVQREHLG--PLASGAHKLV  
RLV + S W++FDV+ AV W ++V+ HL P G H +

Sbjct: 202 RLVRHNASRWESFDVSPAVLRW----TRERLPNYGLAVEVLHLNQTTPRHQGRHVRI

Query: 224 QGAPAGLGEPQLELHTLDRDYGAQGDCDP-----EAPMTEGTR----CCRQEMY  
P GE +L L L +G G P +P G + C R +Y

Sbjct: 258 HQEP---GEDWEQLRPL-LVTFGHDGKGHPLTRRTKRSPRQRGRKRNRCRRHALY

Query: 274 GMKWAKNWWLEPPGFLAYECVGTCQQP 300

+ W +W++ PPG+ AY C G C P

Sbjct: 314 DVGW-NDWIVAPPGYQAYYCHGECFPF 339

tr Q78DH5 Bmp4 protein [Bmp4] [Haplotaxodon microlepis] 4  
Q78DH5\_9CICH a

Score = 66.2 bits (160), Expect = 2e-09

Identities = 60/207 (28%), Positives = 91/207 (43%), Gaps = 25/207

Query: 107 LPPNSELVQAVLRLRFQEPVPKAALHRHGRLSPRSAQARVTV-EWLRVRDDGSNRTS  
+P + L A LRL++ + +A +S A R+ V E L+ G T

Sbjct: 145 IPEDELLSSAELRLYRHQIDEAIADA---ISDDQALHRINVYEVLKAPRPGQLITQ

Query: 166 RLVSVHESGWKAFDVTEAVNFWXXXXXXXXXXXXXXXXXVSVQREHLG--PLASGAHKLV  
RLV + S W++FDV+ AV W ++V+ HL P G H +

Sbjct: 202 RLVRHNASRWESFDVSPAVLRW----TRERLPNYGLAVEVLHLNQTPRHQGRHVRI

Query: 224 QGAPAGLGEPQLELHTLDLRDYGAQGDCDP-----EAPMTEGTR----CCRQEMY  
P GE +L L L +G G P +P G + C R +Y

Sbjct: 258 HQEP---GEDWEQLRPL-LVTFGHDGKGHPLTRRTKRSRQRGRKRNRCRRHALY

Query: 274 GMKWAKNWWLEPPGFLAYECVGTCQQP 300

+ W +W++ PPG+ AY C G C P

Sbjct: 314 DVGW-NDWIVAPPGYQAYYCHGECFPF 339

tr Q78DH3 Bmp4 protein [Bmp4] [Tanganicodus irsacae (Spotfin  
Q78DH3\_TANIR goby cichlid)]

Score = 66.2 bits (160), Expect = 2e-09

Identities = 60/207 (28%), Positives = 91/207 (43%), Gaps = 25/207

Query: 107 LPPNSELVQAVLRLRFQEPVPKAALHRHGRLSPRSAQARVTV-EWLRVRDDGSNRTS  
+P + L A LRL++ + +A +S A R+ V E L+ G T

Sbjct: 145 IPEDELLSSAELRLYRHQIDEAIADA---ISDDQALHRINVYEVLKAPRPGQLITQ

Query: 166 RLVSVHESGWKAFDVTEAVNFWXXXXXXXXXXXXXXXXXVSVQREHLG--PLASGAHKLV  
RLV + S W++FDV+ AV W ++V+ HL P G H +

Sbjct: 202 RLVRHNASRWESFDVSPAVLRW----TRERLPNYGLAVEVLHLNQTPRHQGRHVRI

Query: 224 QGAPAGLGEPQLELHTLDLRDYGAQGDCDP-----EAPMTEGTR----CCRQEMY  
P GE +L L L +G G P +P G + C R +Y

Sbjct: 258 HQEP---GEDWEQLRPL-LVTFGHDGKGHPLTRRTKRSRQRGRKRNRCRRHALY

Query: 274 GMKWAKNWWLEPPGFLAYECVGTCQQP 300

+ W +W++ PPG+ AY C G C P

Sbjct: 314 DVGW-NDWIVAPPGYQAYYCHGECFPF 339

tr Q8JIK2 Bmp4 protein [Bmp4] [Astatoreochromis alluaudi  
Q8JIK2\_ASTAL (Alluaud's haplo)]

Score = 66.2 bits (160), Expect = 2e-09

Identities = 60/207 (28%), Positives = 91/207 (43%), Gaps = 25/207

Query: 107 LPPNSELVQAVLRLRFQEPVPKAAALHRHGRLSPRSAQARVTV-EWLRVRDDGSNRTS  
+P + L A LRL++ + +A +S A R+ V E L+ G T  
Sbjct: 145 IPEDELLSSAELRLYRHQIDEAIADA---ISDDQALHRINVYEVLKAPRPGQLITQ

Query: 166 RLVSVHESGWKAFDVTEAVNFWXXXXXXXXXXXXXVSVQREHLG--PLASGAHKLV  
RLV + S W++FDV+ AV W ++V+ HL P G H +  
Sbjct: 202 RLVGHNVSrwESFDVSPAVLRW----TRERLPNYGLAVEVLHLNQTprHQGRHVRI

Query: 224 QGAPAGLGEPQLELHTLDRDYGAQGDCDP-----EAPMTEGTR----CCRQEMY  
P GE +L L L +G G P +P G + C R +Y  
Sbjct: 258 HQEP---GEDWEQLRPL-LVTFGHDGKGHPLTRRTKRSRQRGRKRNRCRRHALY

Query: 274 GMKWAKNWWLEPPGFLAYECVGTCQQP 300  
+ W +W++ PPG+ AY C G C P  
Sbjct: 314 DVGW-NDWIVAPPGYQAYYCHGECFPF 339

tr Q8JIJ2 Bmp4 protein [Bmp4] [Tilapia rendalli (redbreast  
Q8JIJ2\_9CICH tilapia)]

Score = 66.2 bits (160), Expect = 2e-09

Identities = 60/207 (28%), Positives = 91/207 (43%), Gaps = 25/207

Query: 107 LPPNSELVQAVLRLRFQEPVPKAAALHRHGRLSPRSAQARVTV-EWLRVRDDGSNRTS  
+P + L A LRL++ + +A +S A R+ V E L+ G T  
Sbjct: 145 IPEDELLSSAELRLYRHQIDEAIADA---ISDDQALHRINVYEVLKAPRPGQLITQ

Query: 166 RLVSVHESGWKAFDVTEAVNFWXXXXXXXXXXXXXVSVQREHLG--PLASGAHKLV  
RLV + S W++FDV+ AV W ++V+ HL P G H +  
Sbjct: 202 RLVRHNASRWESFDVSPAVLRW----THERLPNYGLAVEVLHLNQTprHQGRHVRI

Query: 224 QGAPAGLGEPQLELHTLDRDYGAQGDCDP-----EAPMTEGTR----CCRQEMY  
P GE +L L L +G G P +P G + C R +Y  
Sbjct: 258 HQEP---GEDWEQLRPL-LVTFGHDGKGHPLTRRTKRSRQRGRKRNRCRRHALY

Query: 274 GMKWAKNWWLEPPGFLAYECVGTCQQP 300  
+ W +W++ PPG+ AY C G C P  
Sbjct: 314 DVGW-NDWIVAPPGYQAYYCHGECFPF 339

tr Q78DH4 Bmp4 protein [Bmp4] [Ophthalmotilapia nasuta] 4  
Q78DH4\_9CICH 2

Score = 66.2 bits (160), Expect = 2e-09

Identities = 60/207 (28%), Positives = 91/207 (43%), Gaps = 25/207

Query: 107 LPPNSELVQAVLRLRFQEPVPKAAALHRHGRLSPRSAQARVTV-EWLRVRDDGSNRTS  
+P + L A LRL++ + +A +S A R+ V E L+ G T

Sbjct: 145 IPEDELLSSAELRLYRHQIDEAIADA---ISDDQALHRINVYEVLKAPRPGQLITQ

Query: 166 RLVS VHESGWKAFDVTEAVNFWXXXXXXXXXXXXXXXXXSVQREHLG--PLASGAHKLV  
RLV + S W++FDV+ AV W ++V+ HL P G H +

Sbjct: 202 RLV RHNASRWESFDVSPAVLRW----TRERLPNYGLAVEVLHLNQTPRHQGRHVRI

Query: 224 QGAPAGLGEPQLELHTLDLRDYGAQGDCDP-----EAPMTEGTR----CCRQEMY  
P GE +L L L +G G P +P G + C R +Y

Sbjct: 258 HQEP---GEDWEQLRPL-LVTFGHDGKGHPLTRRTKRSPRQRGRKRNRCRRHALY

Query: 274 GMKWAKNWWLEPPGFLAYECVGTCQQP 300

+ W +W++ PPG+ AY C G C P

Sbjct: 314 DVGW-NDWIVAPPGYQAYYCHGECFPF 339

tr Q8JIJ7 Bmp4 protein [Bmp4] [Julidochromis transcriptus] 4  
Q8JIJ7\_9CICH 2

Score = 65.9 bits (159), Expect = 2e-09

Identities = 60/207 (28%), Positives = 91/207 (43%), Gaps = 25/207

Query: 107 LPPNSELVQAVLRLRFQEPVPKAAALHRHGRLSPRSAQARVTV-EWLRVRDDGSNRTS  
+P + L A LRL++ + +A +S A R+ V E L+ G T

Sbjct: 145 IPVDELLSSAELRLYRHQIDEAIADA---ISDDQALHRINVYEVLKAPRPGQLITQ

Query: 166 RLVS VHESGWKAFDVTEAVNFWXXXXXXXXXXXXXXXXXSVQREHLG--PLASGAHKLV  
RLV + S W++FDV+ AV W ++V+ HL P G H +

Sbjct: 202 RLV RHNASRWESFDVSPAVLRW----TRERLPNYGLAVEVLHLNQTPRHQGRHVRI

Query: 224 QGAPAGLGEPQLELHTLDLRDYGAQGDCDP-----EAPMTEGTR----CCRQEMY  
P GE +L L L +G G P +P G + C R +Y

Sbjct: 258 HQEP---GEDWEQLRPL-LVTFGHDGKGHPLTRRTKRSPRQRGRKRNRCRRHALY

Query: 274 GMKWAKNWWLEPPGFLAYECVGTCQQP 300

+ W +W++ PPG+ AY C G C P

Sbjct: 314 DVGW-NDWIVAPPGYQAYYCHGECFPF 339

tr Q8JIJ3 Bmp4 protein [Bmp4] [Tropheus duboisi] 40  
Q8JIJ3\_9CICH al

Score = 65.5 bits (158), Expect = 3e-09

Identities = 60/207 (28%), Positives = 90/207 (43%), Gaps = 25/207

Query: 107 LPPNSELVQAVLRLRFQEPVPKAAALHRHGRLSPRSAQARVTV-EWLRVRDDGSNRTS  
+P + L A LRL++ + +A +S A R+ V E L+ G T  
Sbjct: 145 IPEDELLSSAELRLYRHQIDEAIADA---ISDDQALHRINVYEVLKAPRPGQLITQ

Query: 166 RLVS VHESGWKAFDVTEAVNFWXXXXXXXXXXXXXXXXXVSVQREHLG--PLASGAHKLV  
RLV S W++FDV+ AV W ++V+ HL P G H +  
Sbjct: 202 RLV RH DASRWESFDVSPAVLRW----TRERLPNYGLAVEVLHLNQT PRHQGRHVRI

Query: 224 QGAPAGLGEPQLELHTLDLRDYGAQGDCDP-----EAPMTEGTR----CCRQEMY  
P GE +L L L +G G P +P G + C R +Y  
Sbjct: 258 HQEP---GEDWEQLRPL-LVTFGHDGKGHPLTRRTKRSRPRQRGRKRNRCRRHALY

Query: 274 GMKWAKNWWLEPPGFLAYECVGTCQQP 300  
+ W +W++ PPG+ AY C G C P  
Sbjct: 314 DVGW-NDWIVAPPGYQAYYCHGECPPF 339

tr Q90YJ3 Anti-dorsalizing morphogenetic protein [admp]  
Q90YJ3\_BRARE [Brachydanio rerio  
(Zebrafish) (Danio rerio)]

Score = 65.1 bits (157), Expect = 4e-09

Identities = 63/231 (27%), Positives = 92/231 (39%), Gaps = 63/231

Query: 110 NSELVQAVLRLRFQ-EPVPKAAALHRHGRLSPRSAQARVTVEWLRVRDDGSNRTS---  
+ +++ A L LF+ P L+RH V +V D G S  
Sbjct: 118 SEKILTAELHLFLKLRPKTSIVLNRHHFCQ-----VSVYQVLD SGKKNVSQ GK

Query: 165 SRLVSVHESGWKAFDVTEAVNFWXXXXXXXXXXXXXXXXXVSVQREHLGPLAS-----GA  
SRLV +H +GW+ F +T+AV W +S + +LG L S G+  
Sbjct: 169 SRLVPIHSTGWEVFTITQAVRSW-----MSDEGSNLGLLVSVRTL AGS

Query: 217 KLVRFASQGAPAGLGEPQLELHTLD-----LRDYGAQGDCDPEAPMT-----  
K+VRFAS +P L L T D L D P +P  
Sbjct: 216 KMVRFASGRDHHHSKQPMLVLFTDDGRR AASLEATSKGSDVSPGSPSQPLPSVPAS

Query: 259 -----EGTRCCRQEMYIDLQGMKWAKNWWLEPPGFLAYECVGTCQQP 300  
E C RQ +Y+D + + W+ W++ P G+ AY C G+C P  
Sbjct: 276 RSV D YDERGEKMACQRQPLYVD FEEIGWS-GWIVSPKGYNAYHCKGSCIFP 325

sp P21275 Bone morphogenetic protein 4 precursor (BMP-4) (BMP-2B)  
BMP4\_MOUSE [Bmp4] [Mus  
musculus (Mouse)]

Score = 64.3 bits (155), Expect = 7e-09  
Identities = 59/226 (26%), Positives = 91/226 (40%), Gaps = 32/226

Query: 92 SEASTHLLVFGMEQRLPPNSELVQAVLRLFQEPVPKA-----ALHRHGRLSPRSAQ  
SE+S +F + +P N + A LRLF+E V + HR

Sbjct: 134 SESSAFRFLFNLSS-IPENEVISSAELRLFREQVDQGPDWEQGFHRINIYEVMPKP

Query: 147 VEWLRVRDDGSNRTSLIDSRLVSVHESGWKAFDVTEAVNFWXXXXXXXXXXXXXVS  
G T L+D+RLV + + W+ FDV+ AV W ++

Sbjct: 193 -----PGHLITRLLDTRLVHHNVTRWETFDVSPAVLRW----TREKQPNYGLA

Query: 207 HLGPLASGAHKLVRFASQGAPAGLGE-----PQLEL-----HTLCLRDIYGAQGD  
HL + + VR S+ P G G+ P L HTL R

Sbjct: 241 HLHQTRTHQGQHVRI-SRSLPQGSQDWAQLRPLLVTFGHDGRGHTLTRRRAKRSPK

Query: 255 APMTEGTRCCRQEMYIDLQGMKWAKNWWLEPPGFLAYECVGTCQQP 300  
+ C R +Y+D + W +W++ PPG+ A+ C G C P

Sbjct: 300 RSRKKNKNCRRHSLYVDFSDVGW-NDWIVAPPGYQAFYCHGDCPFP 344

tr Q8JIK0 Bmp4 protein [Bmp4] [Cyprichromis leptosoma] 4  
Q8JIK0\_9CICH a

Score = 64.3 bits (155), Expect = 7e-09  
Identities = 59/207 (28%), Positives = 90/207 (43%), Gaps = 25/207

Query: 107 LPPNSELVQAVLRLFQEPVPKAAALHRHGRLSPRSAQARVTV-EWLRVRDDGSNRTS  
+P + L A LRL++ + +A +S R+ V E L+ G T

Sbjct: 145 IPEDELLSSAELRLYRHQIDEAIADA---ISDDQXLHRINVYEVLKAPRPGQLITQ

Query: 166 RLVSVHESGWKAFDVTEAVNFWXXXXXXXXXXXXXSVQREHLG--PLASGAHKL  
RLV + S W++FDV+ AV W ++V+ HL P G H +

Sbjct: 202 RLVRHNASRWESFDVSPAVLRW----TRERLPNYGLAVEVLHLNQTPRHQGHVRI

Query: 224 QGAPAGLGEPPQLELHTLCLRDIYGAQGDCDP-----EAPMTEGTR----CCRQEMY  
P GE +L L L +G G P +P G + C R +Y

Sbjct: 258 HQEP---GEDWEQLRPL-LVTFGHDGKGHPLTRRTKRSRQRGRKRNRCRRHALY

Query: 274 GMKWAKNWWLEPPGFLAYECVGTCQQP 300  
+ W +W++ PPG+ AY C G C P

Sbjct: 314 DVGW-NDWIVAPPGYQAYYCHGECFP 339

tr Q8JIJ5            **Bmp4 protein [Bmp4] [Oreochromis niloticus (Nile tilapia)**  
Q8JIJ5\_ORENI       **(Tilapia**  
                     **nilotica)]**

Score = 64.3 bits (155), Expect = 7e-09

Identities = 59/207 (28%), Positives = 90/207 (43%), Gaps = 25/207

Query: 107 LPPNSELVQAVLRLRFQEPVPKAAALHRHGRLSPRSAQARVTV-EWLRVRDDGSNRTS  
          +P + L A LRL++ + +A            +S            R+ V E L+       G T

Sbjct: 145 IPEDELLSSAELRLYRHQIDEAIAA---ISHDQGLHRINVYEVLKAPRPGQLITQ

Query: 166 RLVSVHESGWKAFDVTEAVNFWXXXXXXXXXXXXXXXXXSVVQREHLG--PLASGAHKLV  
          RLV + S W++FDV+ AV W                            ++V+ HL P G H +

Sbjct: 202 RLVRHNASRWESFDVSPAVLRW----TRERLPNYGLAVEVLHLNQTTPRHQGRHVRI

Query: 224 QGAPAGLGEPQLELHTLDRDYGAQGDCDP-----EAPMTEGTR----CCRQEMY  
          P GE +L L L +G G P                            +P G + C R +Y

Sbjct: 258 HQEP---GEDWEQLRPL-LVTFGHDGKGHPLTRRTKRSRQRGRKRNRCRRHALY

Query: 274 GMKWAKNWWLEPPGFLAYECVGTCQQP 300

          + W +W++ PPG+ AY C G C P

Sbjct: 314 DVGW-NDWIVAPPGYQAYYCHGECFPF 339

tr Q3ULR1            **5 days embryo whole body cDNA, RIKEN full-length enriched**  
Q3ULR1\_MOUSE       **library,**  
                     **clone:I0C0022P08 product:bone morphogenetic protein 4,**  
                     **full insert sequence [Bmp4] [Mus musculus (Mouse)]**

Score = 64.3 bits (155), Expect = 7e-09

Identities = 59/226 (26%), Positives = 91/226 (40%), Gaps = 32/226

Query: 92 SEASTHLLVFGMEQRLPPNSELVQAVLRLRFQEPVPKA-----ALHRHGRLSPRSAQ  
          SE+S +F + +P N + A LRL+E V +            HR

Sbjct: 134 SESSAFRFLFNLSS-IPENEVISSAELRLFREQVDQGPDWEQGFHRINIYEVMPKP

Query: 147 VEWLRVRDDGSNRTSLIDSRLVSVHESGWKAFDVTEAVNFWXXXXXXXXXXXXXXXXXVS  
          G T L+D+RLV + + W+ FDV+ AV W                            ++

Sbjct: 193 -----PGHLITRLLDTRLVHHNVTRWETFDVSPAVLRW----TREKQPNYGLA

Query: 207 HLGPLASGAHKLVRFASQGAPAGLGE-----PQLEL-----HTLDRDYGAQGD  
          HL + + VR S+ P G G+ P L                            HTL R

Sbjct: 241 HLHQTRTHQGQHVRI-SRSLPQGSQDWAQLRPLLVTFGHDGRGHTLTRRRAKRSPK

Query: 255 APMTEGTRCCRQEMYIDLQGMKWAKNWWLEPPGFLAYECVGTCQQP 300

          + C R +Y+D + W +W++ PPG+ A+ C G C P

Sbjct: 300 RSRKKNKNCRRHSLYVDFSDVGW-NDWIVAPPGYQAFYCHGDCFPF 344

tr Q8UVQ2 Anti-dorsalizing morphogenetic protein [admp]  
Q8UVQ2\_BRARE [Brachydanio rerio  
(Zebrafish) (Danio rerio)]

Score = 63.5 bits (153), Expect = 1e-08

Identities = 61/227 (26%), Positives = 91/227 (40%), Gaps = 55/227

Query: 110 NSELVQAVLRLFQ-EPVPKAALHRHGRLSPRSAQARVTVEWLRVRDDGSNRTSLID  
+ +++ A L LF+ P L+RH Q V + + S L+  
Sbjct: 118 SEKILTAELHLFKLRPKTSIVLNRH-----HFCQVSVYQVLDSSKKNVSQGKKLLS

Query: 169 SVHESGWKAFDVTEAVNFWXXXXXXXXXXXXXXXXXSVQREHLGPLAS-----GAH---  
+H +GW+ F +T+AV W +S + +LG L S G+  
Sbjct: 173 PIHSTGWEVFTITQAVRSW-----MSDEGSNLGLLVSVRTLGSQMDL

Query: 221 FASQGAPAGLGEPQLELHTLDLR-----DYGAQGDCDPEAPMTEGTR--  
FAS +P L L T D R D G P + R  
Sbjct: 220 FASGRDHHHSKQPMVLVFTDDGRRASLEATSKGSDVSPGGSSQPLPSVPASRRSS

Query: 263 -----CCRQEMYIDLQGMKWAKNWWLEPPGFLAYECVGTCQQP 300  
C RQ +Y+D + + W+ W++ P G+ AY C G+C P  
Sbjct: 280 YDERGEKMACQRQPLYVDFFEEIGWS-GWIVSPKGYNAYHCKGSCIFP 325

tr Q8UVQ8 Anti-dorsalizing morphogenetic protein [admp]  
Q8UVQ8\_BRARE [Brachydanio rerio  
(Zebrafish) (Danio rerio)]

Score = 63.2 bits (152), Expect = 1e-08

Identities = 61/227 (26%), Positives = 91/227 (40%), Gaps = 55/227

Query: 110 NSELVQAVLRLFQ-EPVPKAALHRHGRLSPRSAQARVTVEWLRVRDDGSNRTSLID  
+ +++ A L LF+ P L+RH Q V + + S L+  
Sbjct: 118 SEKILTAELHLFKLRPKTSIVLNRH-----HFCQVSVYQVLDSSKKNVSQGKKLLS

Query: 169 SVHESGWKAFDVTEAVNFWXXXXXXXXXXXXXXXXXSVQREHLGPLAS-----GAH---  
+H +GW+ F +T+AV W +S + +LG L S G+  
Sbjct: 173 PIHSTGWEVFTITQAVRSW-----MSDEGSNLGLLVSVRTLGSQMDL

Query: 221 FASQGAPAGLGEPQLELHTLDLR-----DYGAQGDCDPEAPMTEGTR--  
FAS +P L L T D R D G P + R  
Sbjct: 220 FASGRDHHHSKQPMVLVFTDDGRRASLEATSKGSDVSPGGXSQPLPSVPASRRSS



Query: 263 -----CCRQEMYIDLQGMKWAKNWWLEPPGFLAYECVGTCQQP 300  
C RQ +Y+D + + W+ W++ P G+ AY C G+C P  
Sbjct: 280 YDERGEKMACQRQPLYVD FEEIGWS-GWIVSPKGYNAYHCKGSCIFP 325

tr Q8JIJ8 Bmp4 protein [Bmp4] [Haplochromis nyererei] 4  
Q8JIJ8\_9CICH a

Score = 63.2 bits (152), Expect = 1e-08  
Identities = 59/207 (28%), Positives = 90/207 (43%), Gaps = 25/207

Query: 107 LPPNSELVQAVLRLFQEPVPKAALHRHGRLSPRSAQARVTV-EWLRVRDDGSNRTS  
+P + L A LRL++ + +A +S A R+ V E L+ G T  
Sbjct: 145 IPEDELLSSAELRLYRHQIDEAIADA---ISDDQALHRINVYEVLKAPRPGQLITQ

Query: 166 RLVS VHESGWKAFDVTEAVNFWXXXXXXXXXXXXXXXXXSVQREHLG--PLASGAHKLV  
RLV + S W++FDV+ AV W ++V+ HL P G H +  
Sbjct: 202 RLVRHNASRWESFDVSPAVLRW----ARERLPNYGLAVEVLHLNQTTPRHQGRHVRI

Query: 224 QGAPAGLGEPQLELHTLDLRDYGAQGD-----CDPEAPMTEGTR----CCRQEMY  
P GE +L L L +G G +P G + C R +Y  
Sbjct: 258 HQEP---GEDWEQLRPL-LVTFGHDGKGHSLTRRTKRSRQRGRKRNRCRRHALY

Query: 274 GMKWAKNWWLEPPGFLAYECVGTCQQP 300  
+ W +W++ PPG+ AY C G C P  
Sbjct: 314 DVGW-NDWIVAPPGYQAYYCHGECFPF 339

sp Q06826 Bone morphogenetic protein 4 precursor (BMP-4) (BMP-2B) 4  
BMP4\_RAT [Bmp4] 2  
[Rattus norvegicus (Rat)]

Score = 62.8 bits (151), Expect = 2e-08  
Identities = 59/226 (26%), Positives = 89/226 (39%), Gaps = 32/226

Query: 92 SEASTHLLVFGMEQRLPPNSELVQAVLRLFQEPVPKA-----ALHRHGRLSPRSAQ  
SE+S F + +P N + A LRLF+E V + HR  
Sbjct: 134 SESSAFRFFFNLS-IPENEVISSAELRLFREQVDQGPDWEQGFHRINIYEVMPKP

Query: 147 VEWLRVRDDGSNRTSLIDSRLVS VHESGWKAFDVTEAVNFWXXXXXXXXXXXXXXXXXVS  
G T L+D+RLV + + W+ FDV+ AV W ++  
Sbjct: 193 -----PGHLITRLLDTRLVRHNVTRWETFDVSPAVLRW----TREKQPNYGLA

Query: 207 HLGPLASGAHKLVRFASQGAPAGLG-----EPQLEL-----HTLDLRDYGAQGD  
HL + + VR S+ P G G P L HTL R

Sbjct: 241 HLHQTRTHQGQHVRI-SRSLPQGSGNWAQLRPLLVTFGHDGRGHTLTRRRRAKRSPK

Query: 255 APMTEGTRCCRQEMYIDLQGMKWAKNWWLEPPGFLAYECVGTCCQP 300

+ C R +Y+D + W +W++ PPG+ A+ C G C P

Sbjct: 300 RSRKKNKNCRRHSLYVDFSDVGW-NDWIVAPPGYQAFYCHGDCFPF 344

tr Q6AYU9 **Bmp4 protein [Bmp4] [Rattus norvegicus (Rat)]** 40  
Q6AYU9\_RAT al

Score = 62.8 bits (151), Expect = 2e-08

Identities = 59/226 (26%), Positives = 89/226 (39%), Gaps = 32/226

Query: 92 SEASTHLLVFGMEQRLPPNSELVQAVLRLFQEPVPKA-----ALHRHGRLSPRSAQ  
SE+S F + +P N + A LRLF+E V + HR

Sbjct: 134 SESSAFRFFFFNLSS-IPENEVISSAELRLFREQVDQGPDWEQGFHRINIYEVMPKP

Query: 147 VEWLRVRDDGSNRTSLIDSRLVSVHESGWKAFDVTEAVNFWXXXXXXXXXXXXXVS  
G T L+D+RLV + + W+ FDV+ AV W ++

Sbjct: 193 -----PGHLITRLLDTRLVHHNVTRWETFDVSPAVLRW----TREKQPNYGLA

Query: 207 HLGPLASGAHKLVRFASQGAPAGLG-----EPQLEL-----HTLDLRDYGAQGD  
HL + + VR S+ P G G P L HTL R

Sbjct: 241 HLHQTRTHQGQHVRI-SRSLPQGSGNWAQLRPLLVTFGHDGRGHTLTRRRRAKRSPK

Query: 255 APMTEGTRCCRQEMYIDLQGMKWAKNWWLEPPGFLAYECVGTCCQP 300

+ C R +Y+D + W +W++ PPG+ A+ C G C P

Sbjct: 300 RSRKKNKNCRRHSLYVDFSDVGW-NDWIVAPPGYQAFYCHGDCFPF 344

tr Q811S3 **Bone morphogenetic protein 4 [Bmp4] [Rattus norvegicus**  
Q811S3\_RAT **(Rat)]**

Score = 62.8 bits (151), Expect = 2e-08

Identities = 59/226 (26%), Positives = 89/226 (39%), Gaps = 32/226

Query: 92 SEASTHLLVFGMEQRLPPNSELVQAVLRLFQEPVPKA-----ALHRHGRLSPRSAQ  
SE+S F + +P N + A LRLF+E V + HR

Sbjct: 134 SESSAFRFFFFNLSS-IPENEVISSAELRLFREQVDQGPDWEQGFHRINIYEVMPKP

Query: 147 VEWLRVRDDGSNRTSLIDSRLVSVHESGWKAFDVTEAVNFWXXXXXXXXXXXXXVS  
G T L+D+RLV + + W+ FDV+ AV W ++

Sbjct: 193 -----PGHLITRLLDTRLVHHNVTRWETFDVSPAVLRW----TREKQPNYGLA

Query: 207 HLGPLASGAHKLVRFASQGAPAGLG-----EPQLEL-----HTLDLRDYGAQGD

HL + + VR S+ P G G P L HTL R  
Sbjct: 241 HLHQTRTHQGQHVRI-SRSLPQGGSGNWAQLRPLLVTFGHDGRGHTLTRRRRAKRSPK  
Query: 255 APMTEGTRCCRQEMYIDLQGMKWAKNWWLEPPGFLAYECVGTCCQP 300  
+ C R +Y+D + W +W++ PPG+ A+ C G C P  
Sbjct: 300 RSRKKNKNCRRHSLYVDFSDVGW-NDWIVAPPGYQAFYCHGDCPFP 344

tr Q8AYB5 Bone morphogenetic protein 4 (Fragment) [Oryzias  
Q8AYB5\_ORYLA latipes (Medaka  
fish) (Japanese ricefish)]

Score = 62.0 bits (149), Expect = 3e-08  
Identities = 58/216 (26%), Positives = 92/216 (42%), Gaps = 19/216

Query: 95 STHLLVFGMEQRLPPNSELVQAVLRLFQEPVPKAALHRHGRLSPRSAQARVTVEWL  
S HL +P + L A LRL+++ + +A + L+ + E L  
Sbjct: 133 SIHLRFLFNLSSIPEDELLSSAELRLYRQQLGEA--NDDSPNDQGLHRINIYEV

Query: 155 DGSNRTSLIDSRLVSVHESGWKAFDVTEAVNFWXXXXXXXXXXXXXSVQREHLGP  
G T L+D+RLV + S W++FDV+ AV W ++V+ HL  
Sbjct: 191 PGQLITQLLDTRLVHHNASRWESFDVSPAVLRW----TRERLPNYGLAVEILHLNQ

Query: 215 AHKLVRFASQGAPAGLGEPQLELHTLDLRDYGAQGD-----CDPEAPMTEGTR--  
H+ VR S+ GE ++ L L +G G +P G +  
Sbjct: 247 QHRHVRI-SRSLHQEPGEDWDQVRPL-LVTFGHDGKGHSLTRRTKRSPKPRGRKR

Query: 265 RQEMYIDLQGMKWAKNWWLEPPGFLAYECVGTCCQP 300  
R +Y+D + W +W++ PPG+ AY C G C P  
Sbjct: 305 RHTLYVDFSDVGW-NDWIVAPPGYQAYYCHGECFPF 339

tr Q91597 Anti-dorsalizing morphogenetic protein 1 precursor [Xenopus  
Q91597\_XENLA laevis  
(African clawed frog)]

Score = 62.0 bits (149), Expect = 3e-08  
Identities = 59/217 (27%), Positives = 88/217 (40%), Gaps = 38/217

Query: 110 NSELVQAVLRLFQ---EPVPKAALHRHGRLSPRSAQARVTVEWLVRDDGSNRTSL  
N +++ A L LF+ P +A RH Q V + + + L  
Sbjct: 120 NEKILTAELHLFLKLPKPSEQAYFKRH-----HFCQISVYMLVDKNKIQLPQGRKL

Query: 167 LSVHESGWKAFDVTEAVNFWXXXXXXXXXXXXXSVQREHLGPLASGAHKLVRFA  
LV +H SGW+ F +T+AV W + V +LG A ++RFA

Sbjct: 175 LVPIHSSGWEVFSITQAVRAW-----NDESANHGILVTVRNLGG-AQVDPNIIRFA  
Query: 227 PAGLGEPQLELHTLDLR----DYGAQGDCD-----PEAPMTEGTR-----  
          +P L L T D R           Q D           P A P + TR  
Sbjct: 229 HHESKQPMLVLFDTDDGRRGIVSVNNQPDDQLMPLPNVPMAPTSNRTRLGRSVEEDG  
Query: 264 CRQEMYIDLQGMKWAKNWWLEPPGFLAYECVGTCQQP 300  
          R +Y+D + + W+ W++ P G+ AY C G+C P  
Sbjct: 289 QRHPLYVDFEEIGWS-GWIISPRGYNAYHCKGSCFPF 324

sp Q90752 Bone morphogenetic protein 4 precursor (BMP-4) [BMP4]  
BMP4\_CHICK [Gallus  
gallus (Chicken)]

Score = 60.5 bits (145), Expect = 9e-08  
Identities = 62/224 (27%), Positives = 93/224 (41%), Gaps = 31/224

Query: 92 SEASTHLLVFGMEQRLPPNSELVQAVLRLFQEPV--PKAALHRHGRLSPRSAQARV  
SEA VF + +P N + LRL++E V P AA R R+  
Sbjct: 134 SEAPRIRFVFNLS--VPDNEVISSEELRLYREQVEEPSAAWERGFI-----RI  
Query: 149 WLRVRDDGSNR-TSLIDSRLVSVHESGWKAFDVTEAVNFWXXXXXXXXXXXXXVSV  
++ + S T L+D+RLV + + W+ FDV+ AV W + V  
Sbjct: 185 VMKPLSERSQAITRLLDTRLVHHNVTRWETFVDVSPAVIRW--TKDKQPNHGLVIEV  
Query: 208 LGPLASGAHKLVRFASQGAPAGLGEPQLELHTLDLRDYGAQGDCDP-----EAPM  
G H + S+ P G G +L L L +G G +P  
Sbjct: 243 QAQTHQGKHVRI---SRSLPQGHGGDWAQLRPL-LVTFGHDGRGHALTRRARRSPK  
Query: 262 R-----CCRQEMYIDLQGMKWAKNWWLEPPGFLAYECVGTCQQP 300  
R C R +Y+D + W +W++ PPG+ A+ C G C P  
Sbjct: 299 RKNKKNCRHALYVDFSDVGW-NDWIVAPPGYQAFYCHGDCFPF 341

tr 057574 Bone genetic protein 4 (Bone morphogenetic protein  
057574\_BRARE 4) [bmp4]  
[Brachydanio rerio (Zebrafish) (Danio rerio)]

Score = 60.5 bits (145), Expect = 9e-08  
Identities = 48/163 (29%), Positives = 70/163 (42%), Gaps = 17/163

Query: 148 EWLRVRDDGSNRTSLIDSRLVSVHESGWKAFDVTEAVNFWXXXXXXXXXXXXXVSV  
E L+ +G T L+D+RLV + S W++FDV+ AV W V V  
Sbjct: 181 EVLKAPREGQLITQLLDTRLVRHNTSKWESFDVSPAVLRW--TQEKRSNHGLAVEV

Query: 208 LGPLASGAHKLVRFASQGAPAGLGEPQLELHTLTLDRDYGAQGDCDP-----EAPM  
P+ G H V + P E +L L L +G G P +P  
Sbjct: 239 RNPVQKGRHVRVSRSVHPLP---DEEWDQLRPL-LVTFGHDGKSHPLTRRAKRSPK

Query: 262 R----CCRQEMYIDLQGMKWAKNWWLEPPGFLAYECVGTCCQP 300  
+ C R +Y+D + W +W++ PPG+ AY C G C P  
Sbjct: 295 KRNRNCRRHALYVDFSDVGW-NDWIVAPPGYQAYYCHGECFPF 336

tr P87380 Bone morphogenetic protein-4 (Fragment) [bmp4]  
P87380\_BRARE [Brachydanio rerio  
(Zebrafish) (Danio rerio)]

Score = 60.5 bits (145), Expect = 9e-08  
Identities = 48/163 (29%), Positives = 70/163 (42%), Gaps = 17/163

Query: 148 EWLVRDDGSNRTSLIDSRLVSVHESGWKAFDVTEAVNFWXXXXXXXXXXXXXVSV  
E L+ +G T L+D+RLV + S W++FDV+ AV W V V  
Sbjct: 180 EVLKAPREGQLITQLLDTRLVRHNTSKWESFDVSPAVLRW--TQEKRSNHGLAVEV

Query: 208 LGPLASGAHKLVRFASQGAPAGLGEPQLELHTLTLDRDYGAQGDCDP-----EAPM  
P+ G H V + P E +L L L +G G P +P  
Sbjct: 238 RNPVQKGRHVRVSRSVHPLP---DEEWDQLRPL-LVTFGHDGKSHPLTRRAKRSPK

Query: 262 R----CCRQEMYIDLQGMKWAKNWWLEPPGFLAYECVGTCCQP 300  
+ C R +Y+D + W +W++ PPG+ AY C G C P  
Sbjct: 294 KRNRNCRRHALYVDFSDVGW-NDWIVAPPGYQAYYCHGECFPF 335

tr Q28BW9 Novel protein similar to anti-dorsalizing  
Q28BW9\_XENTR morphogenic protein  
[TGas066c03.1-001] [Xenopus tropicalis (Western  
clawed  
frog) (Silurana tropicalis)]

Score = 60.1 bits (144), Expect = 1e-07  
Identities = 58/217 (26%), Positives = 87/217 (40%), Gaps = 38/217

Query: 110 NSELVQAVLRLRFQ---EPVPKAALHRHGRLSPRSAQARVTVEWLVRDDGSNRTSL  
N +++ A L LF+ P +A RH Q V + + + L  
Sbjct: 120 NEKILTAELHLFLKLPKRPSEQAYFKRH-----HFCQISVYLVLDKNKIQLPQGRKL

Query: 167 LVSVHESGWKAFDVTEAVNFWXXXXXXXXXXXXXVSVQREHLGPLASGAHKLVRF  
LV +H SGW+ F +T+AV W + V +LG A ++RFA  
Sbjct: 175 LVPIHSSGWEVFSITQAVRAW-----NDESANHGILVTVRNLGG-AQVDPNIIRFA

Query: 227 PAGLGEPQLELHTLTLR----DYGAQGDCD-----PEAPMTEGTR-----  
                  +P L L T D R                   Q D                   P P + TR  
Sbjct: 229 HHESKQPMLVLFTDDGRRGIVSVNNQPDGQMVPLPNGPFPVPSNRTRISRSVEDDG

Query: 264 CRQEMYIDLQGMKWAKNWWLEPPGFLAYECVGTCQQP 300  
                  R +Y+D + + W+ W++ P G+ AY C G+C P  
Sbjct: 289 QRHPLYVDFEIEIGWS-GWIIISPRGYNAYHCKGSCFPF 324

tr    Q6J3S5                   Bone morphogenetic protein 24B [BMP24B] [Petromyzon  
      Q6J3S5\_PETMA           marinus (Sea  
                              lamprey)]

Score = 60.1 bits (144), Expect = 1e-07  
Identities = 67/287 (23%), Positives = 109/287 (37%), Gaps = 33/28

Query: 45 RADMEKLV---IPAHVRAQYVLLRRSHGDRS--RGKRFSQSFREVAGRFLASEAS  
          RAD E++       +       + V   R + G +   RG   +S   +++       + +  
Sbjct: 103 RADKERVGKDDVDVEEEKEEVAFPREAQGRANTVRGFHHDESTKLSLGQSTEDGT

Query: 100 VFGMEQRLPPNSELVQAVLRLRFQEPV--PKAALHRHGRSLSPRSAQARVTVEWLRVR  
          +F +       +P + E+   A LR+       V P +       L+PR + V  
Sbjct: 163 LFNLS-IPDSEEVTAELRVHHTRVHSPCPSSSPACELAPRLERINVYEVVAPPS

Query: 158 NRTSLIDSRLVSVHESGWKAFDVTEAVNFWXXXXXXXXXXXXXXXXXV-SVQREHLGPLA  
          + L+D+R+V   +ES W+AFDV+ AV+ W                   V V+R   G A  
Sbjct: 222 AASRLLDTRVVRTNESRWEAFDVSPA VSRWTRGSAPNRGFAVEVLPVRRPSGGVAA

Query: 217 KLVRFASQGAPAGLGEPQLELHTLTLRDLR DYGAQGDCDPEAPMTEGTR-----  
                  A +       P   H + R                   D AP T +R  
Sbjct: 282 SEAVLAQPRSGVASLFPDGDGSHQTEPRLLVTFGSDGRAPFTPRSRARRSIGGAPR

Query: 263 -----CCRQEMYIDLQGMKWAKNWWLEPPGFLAYECVGTCQQP 300  
                  C R +Y+D + + W +W++ PPG+ AY C G C P  
Sbjct: 342 KARRKPRYSCRRHALYVDFREVGW-NDWIVAPPGYHAYFCHGECFPF 387

tr    Q2KT33                   Bone morphogenetic protein 4 (Fragment)  
      Q2KT33\_ELECQ           [Eleutherodactylus coqui  
                              (Puerto Rican coqui)]

Score = 59.7 bits (143), Expect = 2e-07  
Identities = 48/205 (23%), Positives = 86/205 (41%), Gaps = 23/205

Query: 107 LPPNSELVQAVLRLRFQEPVPKAALHRHG--RLSPRSAQARVTVEWLRVRDDGSNRT  
 +P N + A LRL++E + G R++ +T +G T  
 Sbjct: 146 IPENEVISSAELRLYREQIEHGPAWEEGFHRINIYEVMTLTA-----NGQMIT

Query: 165 SRLVSVHESGWKAQFDVTEAVNFWXXXXXXXXXXXXXSVSVQREHLGPLASGAHKLVR  
 +RL+ + + W++FDV+ A+ W ++V+ HL + K VR  
 Sbjct: 199 TRLIHHNVTRWESFDVSPAIMRW----TQVKGINHGLAVEVIHLNQTKTYQGKHVR

Query: 225 GAPAGLGE-----PQLELHTLTLRDYG----AQGDCEAPMTEGTRCCCRQEMYID  
 P + P L + D R + ++ P+ + C R +Y+D  
 Sbjct: 255 LLPQDNADWSQMRPLLITFSHDGRGHALTRRSKRSPKQARAKKNKNCRRHSPLYVD

Query: 276 KWAKNWWLEPPGFLAYECVGTCQQP 300  
 W +W++ PPG+ A+ C G C P  
 Sbjct: 315 GW-NDWIVAPPGYQAFYCHGDCPFP 338

tr 013107 BMP4 [bmp4] [Brachydanio rerio (Zebrafish) (Danio  
 013107\_BRARE rerio)]

Score = 59.7 bits (143), Expect = 2e-07

Identities = 47/163 (28%), Positives = 69/163 (42%), Gaps = 17/163

Query: 148 EWLVRDDGSNRTSLIDSRLVSVHESGWKAQFDVTEAVNFWXXXXXXXXXXXXXSVSV  
 E L+ +G T L+D+RLV + S W++FDV+ AV W V V  
 Sbjct: 181 EVLKAPREGQLITQLDTRLVRPNTSKWESFDVSPAFLRW--TQEKRSNHGLAVEV

Query: 208 LGPLASGAHKLVRFASQGAPAGLGEPPQLELHTLTLRDYGAQGDCEP-----EAPM  
 P+ G H V + P E + L L +G G P +P  
 Sbjct: 239 RNPVQKGRHARVSRSVHPLP---NEEWDHVRPL-LVTFGHDGKSHPLTRRAKRSK

Query: 262 R----CCRQEMYIDLQGMKWAKNWWLEPPGFLAYECVGTCQQP 300  
 + C R +Y+D + W +W++ PPG+ AY C G C P  
 Sbjct: 295 KRNRCRRHALYVDFSDVGW-NDWIVAPPGYQAYYCHGECFPF 336

tr Q2KJH1 Hypothetical protein [Bos taurus (Bovine)] 4  
 Q2KJH1\_BOVIN a

Score = 59.7 bits (143), Expect = 2e-07

Identities = 58/227 (25%), Positives = 89/227 (39%), Gaps = 33/227

Query: 92 SEASTHLLVFGMEQRLPPNSELVQAVLRLRFQEPVPKA-----ALHRHGRLSPRSAQ  
 SE S +F + +P N + A LRLF+E V + HR  
 Sbjct: 134 SENSARFLFNLSS-IPENEVISSAELRLRFREQVDQGPDWDQGFHRINIYEVMTKPP

Query: 147 VEWLRVRDDGSNRTSLIDSRLVSVHESGWKAFDVTEAVNFWXXXXXXXXXXXXXVS  
                  G  T L+D+RLV  +  + W+ FDV+ AV  W                  ++  
Sbjct: 193 -----PGHLITRLLDTRLVHHNVTRWETFDVSPAVLRW-----TREKQPNYGLA

Query: 207 HLGPLASGAHKLVRFASQGAPAGLGE-----PQLELHTLDLRDYG-----AQG  
                  HL      +      + VR  S+  P G G+      P L      D R  +  
Sbjct: 241 HLHQTRTHQGQHVRI-SRSLPQGSQDWAQLRPLLVTFGHDGRGHALTRRRRAKRSP

Query: 254 EAPMTEGTRCCRQEMYIDLQGMKWAKNWWLEPPGFLAYECVGTCQQP 300  
                  +      +      C R  +Y+D      + W  +W++ PPG+ A+ C G C  P  
Sbjct: 300 QRARKKNKNCRRHSlyVDFSDVGW-NDWIVAPPGYQAFYCHGDCFPF 345

tr  Q5I4I9                  Bone morphogenetic protein 4 (Fragment) [BMP4] [Bos  
    Q5I4I9\_BOVIN          taurus  
                          (Bovine)]

Score = 59.3 bits (142), Expect = 2e-07  
Identities = 58/227 (25%), Positives = 89/227 (39%), Gaps = 33/227

Query: 92  SEASTHLLVFGMEQRLPPNSELVQAVLRLFQEPVPKAA-----LHRHGRLSPRSAQ  
                  SE S      +F +      +P N  +  A LRLF+E V  +          HR  
Sbjct: 114 SENSARFLFLNLSS-IPENEVISSAELRLFREQVDQGPDWDQDFHRINIYEVMPKP

Query: 147 VEWLRVRDDGSNRTSLIDSRLVSVHESGWKAFDVTEAVNFWXXXXXXXXXXXXXVS  
                  G  T L+D+RLV  +  + W+ FDV+ AV  W                  ++  
Sbjct: 173 -----PGHLITRLLDTRLVHHNVTRWETFDVSPAVLRW-----TREKQPNYGLA

Query: 207 HLGPLASGAHKLVRFASQGAPAGLGE-----PQLELHTLDLRDYG-----AQG  
                  HL      +      + VR  S+  P G G+      P L      D R  +  
Sbjct: 221 HLHQTRTHQGQHVRI-SRSLPQGSQDWAQLRPLLVTFGHDGRGHALTRRRRAKRSP

Query: 254 EAPMTEGTRCCRQEMYIDLQGMKWAKNWWLEPPGFLAYECVGTCQQP 300  
                  +      +      C R  +Y+D      + W  +W++ PPG+ A+ C G C  P  
Sbjct: 280 QRARKKNKNCRRHSlyVDFSDVGW-NDWIVAPPGYQAFYCHGDCFPF 325

tr  Q8MJV5                  Bone morphogenetic protein 4 [sBmp4] [Suncus murinus (House  
    Q8MJV5\_SUNMU          shrew)  
                          (Musk shrew)]

Score = 58.5 bits (140), Expect = 4e-07  
Identities = 58/227 (25%), Positives = 88/227 (38%), Gaps = 33/227



Query: 92 SEASTHLLVFGMEQRLPPNSELVQAVLRLRFQEPVPKA-----ALHRHGRLSPRSAQ  
 SE S F + +P N + A LRLF+E V + HR  
 Sbjct: 134 SENSACFRFFNLSS-IPENEVISSAELRLRFREQVDQGPDWEQGFHRINIYEVMPKP

Query: 147 VEWLRVRDDGSNRTSLIDSRLVSVHESGWKAFDVTEAVNFWXXXXXXXXXXXXXVS  
 G T L+D+RLV + + W+ FDV+ AV W ++  
 Sbjct: 193 -----PGHLITRLLDTRLVHHNVTRWETFDVSPAVLRW----TREKQPNYGLA

Query: 207 HLGPLASGAHKLVRFASQGAPAGLGE-----PQLELHTLDLRDYG-----AQG  
 HL + + VR S+ P G G+ P L D R +  
 Sbjct: 241 HLHQTRTHQGQHVRI-SRSLPQGNQDWAQLRPLLVTFGHDGRGHALTRRRRAKRSP

Query: 254 EAPMTEGTRCCRQEMYIDLQGMKWAKNWWLEPPGFLAYECVGTCQQP 300  
 + + C R +Y+D + W +W++ PPG+ A+ C G C P  
 Sbjct: 300 QRARKKNKNCRRHSYVDFSDVGW-NDWIVAPPGYQAFYCHGDCPFP 345

tr Q1LWW7 Novel protein similar to bone morphogenetic protein  
 Q1LWW7\_BRARE 7 (Bmp7)  
 [RP71-45K5.6-001] [Brachydanio rerio (Zebrafish)  
 (Danio  
 rerio)]

Score = 58.2 bits (139), Expect = 5e-07  
 Identities = 45/169 (26%), Positives = 65/169 (38%), Gaps = 19/169

Query: 148 EWLVRVRDDGSNRTSLIDSRLVSVHESGWKAFDVTEAVNFWXXXXXXXXXXXXXVS  
 E LR + L+D + V + GW AFDVT A N W V  
 Sbjct: 203 EILREKRHREPELVLLDMQSVPAQEGWLAFDVTSASNRWLLHPRSNLGIRLYVET

Query: 208 -----LGPLASGAHKLVRFASQGAPAGLGEPPQLELHTLDLRDYGAQGDCDPE  
 GP + + F + AP P+ HT + P  
 Sbjct: 263 RSWVGLVGRRGPRSKQPFMVTFFRASQAPC--RPPRALKHTNQKTKYDLPHPN

Query: 257 ----MTEGTRCCRQ-EMYIDLQGMKWAKNWWLEPPGFLAYECVGTCQQP 300  
 + G + C++ E+Y+ + W K+WVL P G+ AY C G C P  
 Sbjct: 321 FDQNHSSGRQACKKHELYVSFSDLGW-KDWVLAPTGYSAAYCDGECDDP 368

tr Q90YD6 Bone morphogenetic protein 4 (BMP4) [BMP-4] [Xenopus  
 Q90YD6\_XENTR tropicalis  
 (Western clawed frog) (Silurana tropicalis)]

Score = 57.0 bits (136), Expect = 1e-06  
 Identities = 49/220 (22%), Positives = 90/220 (40%), Gaps = 24/220

Query: 92 SEASTHLLVFGMEQRLPPNSELVQAVLRLFQEPVPKAALHRHG--RLSPRSAQARV  
+E VF + +P N + A LRL++E + G R++ +  
Sbjct: 130 AENGNF RFVFNLS-IPENEVISSAELRLYREQIDHGPAWEEGFHRINIYEVMPKI

Query: 150 LRVRDDGSNRTSLIDSRLVSVHESGWKAFDVTEAVNFWXXXXXXXXXXXXXSVSVQR  
G + L+D+RL+ + + W++FDV+ A+ W +++++  
Sbjct: 188 -----GHMISRLLDTRLIHHNVTQWESFDVSPAIRWTRDKQINHG----LAIEV

Query: 210 PLASGAHKLVRFASQGAPAGLGE-----PQLELHTLDLRDYG----AQGDCEAP  
+ K VR + P + P L + D R + ++ + P  
Sbjct: 238 QTKTYQGKHVRISRLLPQEDADWSQMRPLLITFSHDGRGHALTRRSKRSPKQQR

Query: 261 TRCCRQEMYIDLQGMKWAKNWWLEPPGFLAYECVGTCQQP 300  
C R +Y+D +.W +W++ PPG+ A+ C G C P  
Sbjct: 298 KHCRRHS LYVDFSDVGW-NDWIVAPPGYQAFYCHGDCPFP 336

tr Q2I6C6 Bone morphogenetic protein 4 (Fragment) [Bmp4]  
Q2I6C6\_CARPS [Carollia  
perspicillata (Seba's short-tailed bat)]

Score = 56.6 bits (135), Expect = 1e-06

Identities = 53/212 (25%), Positives = 83/212 (39%), Gaps = 32/212

Query: 107 LPPNSELVQAVLRLFQEPVPKA-----ALHRHGRLSPRSAQARVTVEWLRVRDDGS  
+P N + A LRLF+E V + HR A + G  
Sbjct: 5 IPENEVISSAELRLFREQVDQGPDWERG FHRINIYEVMPKPPAELV-----PGH

Query: 162 LIDSRLVSVHESGWKAFDVTEAVNFWXXXXXXXXXXXXXSVSVQREHLGPLASGAHK  
L+D+RLV + + W+ FDV+ AV W +++++ HL + +  
Sbjct: 57 LLDTRLVHHNVTRWETFDVSPA VLRW----TREKQPNYGLAIEVTHLHQTRTHQGG

Query: 222 ASQGAPAGLGE-----PQLELHTLDLRDYG-----AQGDCEAPMTEGTRCC  
S+ P G G+ P L D R + P+ + C  
Sbjct: 113 -SRSLPQGS GDWAQLRPLLVTFGHDGRGHALTRRRRAKRSPKHHPQRARKKNKNCR

Query: 269 YIDLQGMKWAKNWWLEPPGFLAYECVGTCQQP 300  
Y+D + W +W++ PPG+ A+ C G C P  
Sbjct: 172 YVDFSDVGW-NDWIVAPPGYQAFYCHGDCPFP 202

tr Q9MZV5 Bone morphogenetic protein 4 (Fragment) [bmp4]  
Q9MZV5\_CANFA [Canis familiaris  
(Dog)]

Score = 56.6 bits (135), Expect = 1e-06  
Identities = 58/227 (25%), Positives = 89/227 (39%), Gaps = 33/227

```
Query: 92  SEASTHLLVFGMEQRLPPNSELVQAVLRLFQEPVPK-----AALHRHGRLSPRSAQ
          SE S    +F +    +P N +  A LRLF+E V +          HR
Sbjct: 62  SENSAFRFLFNLSS-IPENEVISSAELRLFREQVNQDPDWEQGFHRINIYEVMPKP

Query: 147 VEWLRVRDDGSNRTSLIDSRLVSVHESGWKAFDVTEAVNFWXXXXXXXXXXXXXVS
          G    T L+D+RLV  + + W+ FDV+ AV  W          ++
Sbjct: 121 -----PGHLITRLLDTRLVHHNVTRWETFDVSPAVLRW----TREKQPNYGLA

Query: 207 HLGPLASGAHKLVRFASQGAPAGLGE-----PQLEL-----HTLDLRDYGAQG-
          HL    +    + VR S+  P G G+    P L          H L R    +
Sbjct: 169 HLHQTRTHQGQHVRI-SRSLPQGSQDWAQLRPLLVTFGHDGRGHALTRRQRAKRSP

Query: 254 EAPMTEGTRCCRQEMYIDLQGMKWAKNWWLEPPGFLAYECVGTCQQP 300
          +    +    C R  +Y+D    + W  +W++ PPG+ A+ C G C  P
Sbjct: 228 QRARKKNKNCCRHSLYVDFSDVGW-NDWIVAPPGYQAFYCHGDCFPF 273
```

sp P12644 Bone morphogenetic protein 4 precursor (BMP-4) (BMP-  
BMP4\_HUMAN 2B) [BMP4]  
[Homo sapiens (Human)]

Score = 56.2 bits (134), Expect = 2e-06  
Identities = 58/227 (25%), Positives = 89/227 (39%), Gaps = 33/227

```
Query: 92  SEASTHLLVFGMEQRLPPNSELVQAVLRLFQEPVPKA-----ALHRHGRLSPRSAQ
          SE S    +F +    +P N +  A LRLF+E V +          HR
Sbjct: 133 SENSAFRFLFNLSS-IPENEVISSAELRLFREQVDQGPDWERGFHRINIYEVMPKP

Query: 147 VEWLRVRDDGSNRTSLIDSRLVSVHESGWKAFDVTEAVNFWXXXXXXXXXXXXXVS
          G    T L+D+RLV  + + W+ FDV+ AV  W          ++
Sbjct: 192 -----PGHLITRLLDTRLVHHNVTRWETFDVSPAVLRW----TREKQPNYGLA

Query: 207 HLGPLASGAHKLVRFASQGAPAGLG-----EPQLELHTLDLRDYG----AQGDGCDP
          HL    +    + VR S+  P G G    P L    D R +    +    P
Sbjct: 240 HLHQTRTHQGQHVRI-SRSLPQGSQDWAQLRPLLVTFGHDGRGHALTRRRRAKRSP

Query: 254 EAPMTEGTRCCRQEMYIDLQGMKWAKNWWLEPPGFLAYECVGTCQQP 300
          +    +    C R  +Y+D    + W  +W++ PPG+ A+ C G C  P
Sbjct: 299 QRARKKNKNCCRHSLYVDFSDVGW-NDWIVAPPGYQAFYCHGDCFPF 344
```

tr Q91703 Bone morphogenetic protein 4 [BMP-4] [Xenopus]

Q91703\_XENLA                    **laevis (African  
clawed frog)]**

Score = 56.2 bits (134), Expect = 2e-06

Identities = 50/220 (22%), Positives = 91/220 (41%), Gaps = 24/220

Query: 92 SEASTHLLVFGMEQRLPPNSELVQAVLRLFQEPVPKAALHRHG--RLSPRSAQARV  
          +E            VF +    +P N + A LRL++E +            G R++    +  
Sbjct: 130 AENGNFREFVFNLS-IPENEVISSAELRLYREQIDHGPAWDEGFHRINIYEVMPKI

Query: 150 LRVRDDGSNRTSLIDSRLVSVHESGWKAFDVTEAVNFWXXXXXXXXXXXXXVSVQR  
          L +            NR L+D+RL+    + + W++FDV+ A+ W            ++++  
Sbjct: 189 LMI-----NR--LLDTRLIHHNVTQWESFDVSPAIMRWTRDKQINHG----LAIEV

Query: 210 PLASGAHKLVRFASQGAPAGLGE-----PQLELHTLDRDYG-----AQGDCEPEAP  
          + K VR +    P    +    P L + D R +    ++    + P  
Sbjct: 238 QTKTHQGKHVRISRSLLPQEDADWSQMRPLLITFSHDGRGHALTRRSKRSPKQQR

Query: 261 TRCCRQEMYIDLQGMKWAKNWVLEPPGFLAYECVGTCQQP 300  
          C R +Y+D    + W +W++ PPG+ A+ C G C P  
Sbjct: 298 KHCRRHSLYVDFSDVGW-NDWIVAPPGYQAFYCHGDCPFP 336

tr    Q4SSG4                    **Chromosome undetermined SCAF14443, whole genome  
Q4SSG4\_TETNG                shotgun sequence.  
                              (Fragment) [GSTENG00013441001] [Tetraodon  
                              nigroviridis  
                              (Green puffer)]**

Score = 56.2 bits (134), Expect = 2e-06

Identities = 42/157 (26%), Positives = 62/157 (39%), Gaps = 23/157

Query: 162 LIDSRLVSVHESGWKAFDVTEAVNFWXXXXXXXXXXXXXVSVQREHL-----  
          L+D + V    + GW AFDVT A N W            V + +  
Sbjct: 201 LLDVQSVFAGQEGWLAFDVTTASNHWLLNPRSNLGRIRLYVETEEDRSLGAGWIGLV

Query: 210 PLASGAHKLVRFASQGAP-----AGLGEPQLELHTLDRDYGAQGDCEPEAPMTEG  
          P +            + F    P    A    P+ +    DL    Q    ++P+ G  
Sbjct: 261 PRSKQPFMVTFEFRENQVPCRPPRAAKPHPRKKKPKYDLPVPSIQN----KSPINS

Query: 265 RQ-EMYIDLQGMKWAKNWVLEPPGFLAYECVGTCQQP 300  
          ++ E+Y+    + W K+WVL PPG+ AY C G C P  
Sbjct: 317 KKHELYVSFSDLGW-KDWVLAPPGYSAYYCDGECFYP 352

tr    Q6PAF3                    **LOC397874 protein [LOC397874] [Xenopus laevis**

Q6PAF3\_XENLA (African clawed  
frog)]

Score = 56.2 bits (134), Expect = 2e-06

Identities = 50/220 (22%), Positives = 91/220 (41%), Gaps = 24/220

Query: 92 SEASTHLLVFGMEQRLPPNSELVQAVLRLFQEPVPKAALHRHG--RLSPRSAQARV  
+E VF + +P N + A LRL++E + G R++ +  
Sbjct: 130 AENGFRFVFNLS-IPENEVISSAELRLYREQIDHGPAWDEGFHRINIYEVMPKI

Query: 150 LRVRDDGSNRTSLIDSRLVSVHESGWKAFDVTEAVNFWXXXXXXXXXXXXXSVQR  
L + NR L+D+RL+ + + W++FDV+ A+ W ++++  
Sbjct: 189 LMI-----NR--LLDTRLIHHNVTQWESFDVSPAIMRWTRDKQINHG----LAIEV

Query: 210 PLASGAHKLVRFASQGAPAGLGE-----PQLELHTLDLRDYG----AQGDCEAP  
+ K VR + P + P L + D R + ++ + P  
Sbjct: 238 QTKTHQGKHVRISRSLPQEDADWSQMRPLLITFSHDGRGHALTRRSKRSPKQQR

Query: 261 TRCCRQEMYIDLQGMKWAKNWWLEPPGFLAYECVGTCQQP 300  
C R +Y+D + W +W++ PPG+ A+ C G C P  
Sbjct: 298 KHCRRHS LYVDFSDVGW-NDWIVAPPGYQAFYCHGDCPFP 336

tr . Q53XC5 Full-length cDNA clone CS0DI018YL16 of Placenta of  
Q53XC5\_HUMAN Homo sapiens  
(human) (Full-length cDNA clone CS0DC002YH22 of  
Neuroblastoma of Homo sapiens) [Homo sapiens  
(Human)]

Score = 56.2 bits (134), Expect = 2e-06

Identities = 58/227 (25%), Positives = 89/227 (39%), Gaps = 33/227

Query: 92 SEASTHLLVFGMEQRLPPNSELVQAVLRLFQEPVPKA-----ALHRHGRLSPRSAQ  
SE S +F + +P N + A LRL+E V + HR  
Sbjct: 133 SENSARFLFNLS-IPENEVISSAELRLFREQVDQGPDWERGFHRINIYEVMPK

Query: 147 VEWLVRDDGSNRTSLIDSRLVSVHESGWKAFDVTEAVNFWXXXXXXXXXXXXXVS  
G T L+D+RLV + + W+ FDV+ AV W ++  
Sbjct: 192 -----PGHLITRLLDTRLVHHNVTRWETFDVSPAVLRW----TREKQPNYGLA

Query: 207 HLGPLASGAHKLVRFASQGAPAGLG-----EPQLELHTLDLRDYG----AQGDCEP  
HL + + VR S+ P G G P L D R + + P  
Sbjct: 240 HLHQTRTHQGQHVRI-SRSLPQGSGNWAQLRPLLVTFGHDGRGHALTRRRRAKRSP

Query: 254 EAPMTEGTRCCRQEMYIDLQGMKWAKNWWLEPPGFLAYECVGTCQQP 300  
+ + C R +Y+D + W +W++ PPG+ A+ C G C P  
Sbjct: 299 QRARKKNKNCRRHS LYVDFSDVGW-NDWIVAPPGYQAFYCHGDCPFP 344

tr 073818 Bone morphogenetic protein 4 [BMP-4] [Xenopus  
073818\_XENLA laevis (African  
clawed frog)]

Score = 55.8 bits (133), Expect = 2e-06

Identities = 47/205 (22%), Positives = 86/205 (41%), Gaps = 23/205

Query: 107 LPPNSELVQAVLRLRFQEPVPKAAALHRHG--RLSPRSAQARVTVEWLRVRDDGSNRT  
+P N + A LRL++E + G R++ + L + NR  
Sbjct: 144 IPENEVISSAELRLYREQIDHGPAWDEGFHRINIYEVMPKPIAANGLMI-----NR-

Query: 165 SRLVSVHESGWKAFDVTEAVNFWXXXXXXXXXXXXXXXXXVSVQREHLGPLASGAHKLVR  
+RL+ + + W++FDV+ A+ W ++++ HL + K VR  
Sbjct: 197 TRLIHNVNQWESFDVSPAIMRWTRDKQINHG----LAIEVIHLNQTKTHQGHVR

Query: 225 GAPAGLGE-----PQLELHTLRLRDYG----AQGDCEPEAPMTEGTRCCRQEMYID  
P + P L + D R + ++ + P + C R +Y+D  
Sbjct: 253 LLPQEDADWSQMRPLLITFSHDGRGHALTRRSKRSPKQQRPRKKNKHCRHSLYVD

Query: 276 KWAKNWWLEPPGFLAYECVGTCQQP 300  
W +W++ PPG+ A+ C G C P  
Sbjct: 313 GW-NDWIVAPPGYQAFYCHGDCPFP 336

tr Q6J3S6 Bone morphogenetic protein 24A [BMP24A] [Petromyzon  
Q6J3S6\_PETMA marinus (Sea  
lamprey)]

Score = 55.5 bits (132), Expect = 3e-06

Identities = 81/291 (27%), Positives = 114/291 (39%), Gaps = 50/29

Query: 54 PAHVRAQYVVLRLRS-HGDRSRGKRFSQSFREVAGRFLASEASTHLLVFGME--QR  
P V Y++ L R+ HG S + + + R AS+A+T E +  
Sbjct: 74 PGAVVPPYMLQLYRALHGAHSGARDVGRPLDRLVAR-PASQANTVRSFHHDESAEH

Query: 111 SELVQAVLRLRFQ-----EPVPKAAALH--RHGRLSRSAQA-RVTV-EWLR-VRD  
S A LF E + A LH R SP SA R+ V E LR  
Sbjct: 133 SGDSTARLLFNVSIPDGEVITSaelhvYRERLSSPASAGLHRINVYEVLRPAAA

Query: 159 RTSLIDSRLVSVHESGWKAFDVTEAVNFWXXXXXXXXXXXXXXXXXVSVQREHLGPLASG  
L+D+R+V S W+ FDV+ A W + V+ +HL  
Sbjct: 193 IARLLDTRVVHSGRSEWERFDVSPAAVRWAATKEPNHG----LLVEVQHLDGGTPE

Query: 219 VRF-----ASQGAPAGLGEPQLEL-----HTLDLRDYGAQGDCD  
VR AS+G G G PQL H RD G  
Sbjct: 249 VRIGRSLHAEAVAAAARDGASEGGDGGEGWPQLRPLLVTFGHDGKTRDEGTLLRPR

Query: 256 --PMTEGTR---CCRQEMYIDLQGMKWAKNWWLEPPGFLAYECVGTCQQP 300  
P G R C R +Y+D + W +W++ PPG+ A+ C G C P  
Sbjct: 309 SRPNKGGRGRGRGQCARYPLYVDFSDVGW-NDWIVAPPGYNAFFCQGECHFP 358

tr Q2VEW5 Bone morphogenetic protein 4 [Didelphis albiventris  
Q2VEW5\_DIDAL (White-eared  
opossum)]

Score = 55.5 bits (132), Expect = 3e-06  
Identities = 53/215 (24%), Positives = 84/215 (39%), Gaps = 38/215

Query: 107 LPPNSELVQAVLRLFQEPVPKAA-----LHR---HGRLSPRSAQARVTVEWLRVRD  
+P N + A LRL++E V + + HR + + P +A  
Sbjct: 149 IPENEVISSAELRLYREQVGQSDWELGFHRINIYEVMPKPPAASG-----

Query: 159 RTSLIDSRLVSVHESGWKAFDVTEAVNFWXXXXXXXXXXXXXXXXXSVQREHLGPLASG  
T L+D+RLV + + W++FDV+ AV W + V H G  
Sbjct: 198 ITRLIDTRLVHHNVTQWESFDVSPAVLRWTQDKQPNHGLA--IEVTHLHQRRTHQG

Query: 219 VRFASQGAPAGLGE-----PQLELHTLDLRDYGA-----QGDCDPEAPMTEGT  
+ S+ P G + P L D R + P+ P +  
Sbjct: 256 I---SRSLPQGAADWAQFRPLLVTFGHDGRGHALIRHRAKRSPKHHPQRPRKSK

Query: 266 QEMYIDLQGMKWAKNWWLEPPGFLAYECVGTCQQP 300  
+Y+D + W +W++ PPG+ A+ C G C P  
Sbjct: 313 HPLYVDFSDVGW-NDWIVAPPGYHAFYCQGDCEFP 346

sp P30885 Bone morphogenetic protein 4 precursor (BMP-4) [bmp4]  
BMP4\_XENLA [Xenopus  
laevis (African clawed frog)]

Score = 54.7 bits (130), Expect = 5e-06  
Identities = 45/205 (21%), Positives = 85/205 (41%), Gaps = 23/205

Query: 107 LPPNSELVQAVLRLFQEPVPKAAALHRHG--RLSPRSAQARVTVEWLRVRDDGSNRT  
+P N + A LRL++E + G R++ +T +G  
Sbjct: 145 IPENEVISSAELRLYREQIDHGPAWDEGFHRINIYEVMPKPIA-----NGHMIN

Query: 165 SRLVSVHESGWKAFDVTEAVNFWXXXXXXXXXXXXXXXXXSVQREHLGPLASGAHKLVR

+R++  +  +  W++FDV+  A+  W                  ++++  HL      +  K  VR  
Sbjct: 198  TRVIHHNVTQWESFDVSPAIMRWTLDKQINHG----LAIEVIHLNQTKTYQGKHVR  
  
Query: 225  GAPAGLGE-----PQLELHTLDLRDYG----AQGDCDPEAPMTEGTRCCRQEMYID  
          P      +      P  L      +  D  R  +      ++      +  P  +      C  R  +Y+D  
Sbjct: 254  LLPQKDADWSQMRPLLITFSHDGRGHALTRRSKRSPKQQRPRKKNKHCRRHSlyVD  
  
Query: 276  KWAKNWVLEPPGFLAYECVGTCQQP  300  
          W  +W++  PPG+  A+  C  G  C  P  
Sbjct: 314  GW-NDWIVAPPGYQAFYCHGDCPFP  337

sp      Q29607                  Bone morphogenetic protein 4 precursor (BMP-4) [BMP4]  
      BMP4\_DAMDA              [Dama dama  
                              (Fallow deer) (Cervus dama)]

Score = 54.3 bits (129), Expect = 7e-06  
Identities = 56/227 (24%), Positives = 87/227 (38%), Gaps = 34/227

Query: 92  SEASTHLLVFGMEQRLPPNSELVQAVLRLFQEPVPKA-----ALHRHGRLSPRSAQ  
          SE  S      +F  +      +P  N  +      A  LR  F+E  V  +          HR  
Sbjct: 134  SENSAFRFLFNLS--IPENQVISTAELRDFREQVDQGPDWERGFRINIYEVMPKPP  
  
Query: 147  VEWLRVRDDGSNRTSLIDSRLSVHESGWKAFDVTEAVNFWXXXXXXXXXXXXXXXXXVS  
          G      T  L+D+RLV  +  +  W+  FDV+  AV  W                  ++  
Sbjct: 192  -----PGHLITRLLDTRLVHHNVTRWETFDVSPAFLRW----TREKQPNYGLA  
  
Query: 207  HLGPLASGAHKLVRFASQGAPAGLGE-----PQLELHTLDLRDYG-----AQG  
          HL      +      +  VR  S+  P  G  G+      P  L      D  R  +  
Sbjct: 240  HLHQTRTHQGQHVRISRSLPQSGDWAQLRPLLVTFGHDGRGHALTRHRRAKRSP  
  
Query: 254  EAPMTEGTRCCRQEMYIDLQGMKWAKNWVLEPPGFLAYECVGTCQQP  300  
          +      +      C  R  +Y+D  +  W  +W++  PPG+  A+  C  G  C  P  
Sbjct: 299  QRARKKNKNCRRHSlyVDFSDVGW-NDWIVAPPGYQAFYCHGDCPFP  344

tr      Q90Y82                  LjBmp2/4a (Fragment) [LjBmp2/4a] [Lampetra japonica  
      Q90Y82\_LAMJA              (Japanese  
                              lamprey) (Entosphenus japonicus)]

Score = 53.9 bits (128), Expect = 9e-06  
Identities = 59/229 (25%), Positives = 87/229 (37%), Gaps = 53/229

Query: 107  LPPNSELVQAVLRLFQEPVP---KAALHR---HGRLSPRSAQARVTVEWLRVRDDG  
          +P      +      A  L  +++E  +      +AALHR      +      L  P  +A          DG



Sbjct: 3 IPDGEVITSAELHVVYRERLSGPARAALHRINVYEVLRPAAA-----DG  
Query: 161 SLIDSRLVSVHESGWKAFDVTEAVNFWXXXXXXXXXXXXXSVQREHLGPLASGAH  
L+D+R+V S W+ FDV+ A W + V+ HL  
Sbjct: 50 RLLDTRVVHSGRSEWERFDVSPA AVRW----AAARAPNHGLLVEVHHLDDGGTPEKR  
Query: 221 F-----ASQGAPAGLGEPQLEL-----HTLDLRDYGAQGDCDPE  
A +G G G PQL H RD G P+  
Sbjct: 106 IGRSLHAEAVAAAARDGAGEGGDGGEGWPQLRPLLVTFGHDGKTRDEGTLLRPRPK  
Query: 256 PMTEGTR----CCRQEMYIDLQGMKWAKNWWLEPPGFLAYECVGTCQQP 300  
P G R C R +Y+D + W +W++ PPG+ A+ C G C P  
Sbjct: 166 PNKGGRGRGQCARYPLYVDFSDVGW-NDWIVAPPGYNAFFCQGECHFP 213

tr Q1PHR7 Bone morphogenetic protein 2/4 [Saccoglossus  
Q1PHR7\_SACKO kowalevskii]

Score = 53.5 bits (127), Expect = 1e-05

Identities = 41/145 (28%), Positives = 61/145 (42%), Gaps = 11/145

Query: 162 LIDSRLVSVHESGWKAFDVTEAVNFWXXXXXXXXXXXXXSVQREHLGPLASGAH-  
LIDS +V + S W++FD+ AV W + V+ H + H  
Sbjct: 223 LIDSSVVDIRNSSWESFDIRPAVARW----IAHPEENYGLEVELTHTKNGQASPHQ  
Query: 218 LVRFASQGAPAGLGE-PQLELHTLD-LRDYGAQGDCDPEAPMTEGTRCCCRQEMYID  
L R + A E P L T D R ++ D A C R E+Y+D  
Sbjct: 279 LRRSDTSNAEEWQSERPLLVTFTDDGKRQPQRSKRQSDKRARRRLKLNCKRHELYVD  
Query: 276 KWAKNWWLEPPGFLAYECVGTCQQP 300  
W +W++ PPG+ A+ C G C P  
Sbjct: 339 GW-NDWIVAPPGYHAFYCHGECPPF 362

tr Q2L6L2 Bone morphogenic protein-4 [BMP-4] [Meriones  
Q2L6L2\_MERUN unguiculatus  
(Mongolian jird) (Mongolian gerbil)]

Score = 53.1 bits (126), Expect = 2e-05

Identities = 57/223 (25%), Positives = 87/223 (39%), Gaps = 23/223

Query: 92 SEASTHLLVFGMEQRLPPNSELVQAVLRLFQEPVPKAALHRHGRLSPRSAQARVTV  
SE S +F + +P N + A LRLF+E V + G P + +  
Sbjct: 134 SENSARFLFNLSS-IPENEVVSSAELRLFREQVDQGPDWERG-FHPINIYEVMPK

Query: 152 VRDDGSNRTSLIDSRLVSVHESGWKAFDVTEAVNFWXXXXXXXXXXXXXVSVQREH  
V G T L+D+RLV + + W+ F+V+ V W + V H  
Sbjct: 192 V--PGHFITRLLDTRLVHHNVTRWETFNVS PGVLRWTQENQPNYGLA--IEVIHFH

Query: 212 ASGAHKLVRFASQGAPAGLGE-----PQLEL-----HTLCLR DYGAQG-DCDPE  
G H + S+ P G+ P L HTL R + P+  
Sbjct: 248 HQGQHVRI---SRSLPQQSGDWAQLRPLLVTFGHDGRGHTLTRRRRAKRSLKHHHPQ

Query: 259 EGTRCCRQEMYIDLQGMKWAKNWWLEPPGFLAYECVGTCQQPP 301  
+ C R +Y+D + W +W++ PPG+ A+ C G C PP  
Sbjct: 305 KSKNCRRHSLYVDFSDVGW-NDWIVAPPGYQAFYCHGDCPFPP 346

tr Q9VQG9 CG16987-PA, isoform A (Cg16987-pb, isoform b)  
Q9VQG9\_DROME (GH14433p) [Alp23B]  
[Drosophila melanogaster (Fruit fly)]

Score = 53.1 bits (126), Expect = 2e-05  
Identities = 33/109 (30%), Positives = 53/109 (48%), Gaps = 20/109

Query: 261 TRCCRQEMYIDLQGMKWAKNWWLEPPGFLAYECVGTCQ---QPPEALAFNWPFL--  
T CCR+ +YI + + W+ NW+L+P G+ AY C G+C +A + + +  
Sbjct: 481 TECCREHLYISFRDIGWS-NWILKPEGYNAYFCRGSCSSVASVTQAASHHSSIMKI

Query: 312 GPRQ-----CIASETASLPMIVSIKEGGRTRPQVVSLPNMRVQKCSC 353  
G + C A + +SL ++V T V +LPNM V+ C C  
Sbjct: 540 GANKSLELVPCCTAKQYSSLQLVMDSSNTAT---VKTLPNMVVESC GC 585

sp 008717 Inhibin beta E chain precursor (Activin beta-E  
INHBE\_MOUSE chain) [Inhbe] [Mus  
musculus (Mouse)]

Score = 52.8 bits (125), Expect = 2e-05  
Identities = 33/121 (27%), Positives = 54/121 (44%), Gaps = 27/121

Query: 251 CDPEAPMTEGTRCCRQEMYIDLQGMKWAKNWWLEPPGFLAYECVGTCQ-----QPP  
C+PE P+ CCR++ Y+D Q + W ++W+L+P G+ C G C P  
Sbjct: 240 CEPETPL-----CCRRDHYVDFQELGW-RDWILQPEGYQLNYCSGQCPHLAGSPG

Query: 306 FN-----WPFLGPRQCIASETASLPMIVSIKEGGRTRPQVVSLPNMRVQ  
F+ WP G C+ + L ++ G + V P+M V+  
Sbjct: 294 FHSVAVFSLLKANNPWP-AGSSCCVPTARRPLSLLYLDHNGNVVKTDV---PDMVVE

Query: 354 A 354

+  
Sbjct: 350 S 350

tr Q91XH3 Inhibin beta E [Inhbe] [Mus musculus (Mouse)] 3!  
Q91XH3\_MOUSE a:

Score = 52.8 bits (125), Expect = 2e-05  
Identities = 33/121 (27%), Positives = 54/121 (44%), Gaps = 27/121

Query: 251 CDPEAPMTEGTRCCRQEMYIDLQGMKWAKNWWLEPPGFLAYECVGTCQ-----QPP  
C+PE P+ CCR++ Y+D Q + W ++W+L+P G+ C G C P  
Sbjct: 240 CEPETPL-----CCRRDHYVDFQELGW-RDWILQPEGYQLNYCSGQCPPHLAGSPG

Query: 306 FN-----WPFLGPRQCIASETASLPMIVSIKEGGRTRPQVVSLPNMRVQ  
F+ WP G C+ + L ++ G + V P+M V+  
Sbjct: 294 FHSAVFSLKANNPWP-AGSSCCVPTARRPLSLLYLDHNGNVVKTDV---PDMVVE

Query: 354 A 354  
+  
Sbjct: 350 S 350

tr Q9PVK1 Anti-dorsalizing morphogenetic protein [ADMP]  
Q9PVK1\_CHICK [Gallus gallus  
(Chicken)]

Score = 52.4 bits (124), Expect = 3e-05  
Identities = 57/208 (27%), Positives = 82/208 (39%), Gaps = 41/208

Query: 123 EPVPKAALHRHGRLSPRSAQARVTVEWLRV-----RDDGSNRTSLIDSRLVS  
E + A LH RL PR+A+ + +V D L+ +RL+S  
Sbjct: 102 EKILTAELHLF-RLWPRAAEGPRRHFCQVSVYQILDESEPDSPEGQKLLATRLLS

Query: 174 GWKAFDVTEAVNFWXXXXXXXXXXXXXSVQREHLGPLASGAHKLVRFASQGAPAG  
GW+ F +T+AV W V LG A A V+FAS G  
Sbjct: 161 GWEVFAITQAVRDWTQDESSNRGLLVTV----HGLGGSALAE-PAVQFASSGDHHE

Query: 234 QLELHTLDLRDYGAQGDCDPEAPM-----TEGTR-----CCRQEM  
L L T D G +G P A + G R C R +  
Sbjct: 216 MLVLFT----DDGRRGASLPMAGVPASQPRDFPAKLSGPRSARSLDRLQPCQRHPL

Query: 273 QGMKWAKNWWLEPPGFLAYECVGTCQQP 300  
+ + W+ W++ P G+ AY C G+C P  
Sbjct: 272 EEIGWS-GWIIISPRGYNAYHCRGSCPFP 298

tr Q9PWR8 Activin beta B subunit precursor [Carassius auratus  
Q9PWR8\_CARAU (Goldfish)]

Score = 52.0 bits (123), Expect = 3e-05

Identities = 79/353 (22%), Positives = 131/353 (37%), Gaps = 66/35

Query: 42 VLDRADMEKLVIPAHV--RAQYVVLRRSHGDRSR--GKRFSQSFREVAGRFLASE  
+L+R M + H +A V LR+ H + R G+ +F A E

Sbjct: 66 ILNRLQMRERPNIHPIPKAAMVTALRKLHAGKVREDGRVEIPNFDGHAAHNEVQE

Query: 98 LLVFGMEQRLPPNSELVQAVLRLFQEP---VPKAALHRHGRLSP----RSAQARVT  
++ F + P+ + ++ V +A L + +L P + + +VT

Sbjct: 126 IISFAESDDVTPSKSSLYFLISNEGNQONLYVLQANLWLYFKLLPGTQEKGLRRKVT

Query: 151 RVRDDGSNRTSLIDSRVSVHESGWKAFDVTEAVNFWXXXXXXXXXXXXXVSVQRE  
G N + + V + SGW F V+EAV RE

Sbjct: 186 SYEPGGQNVHWPMMEKRVELKRSGWHTFPVSEAV-----RE

Query: 211 LASGAHKLVRFASQGAPAG-----LGEPQLELHTLDLRDYGAQGDCDP-----E  
G + + +G A L +P H L Q D E

Sbjct: 226 --GGRRQDLDIHCEGCEAANVLPILVDPSPSHRPFLVVRAQQADSKHRIRKRGLE

Query: 259 EGTRCCRQEMYIDLQGMKWAKNWVLEPPGFLAYECVGTCQQ-----PPEALAFNWP  
G CCRQ+ YID + + W +W++ P G+ C G+C P A +F+

Sbjct: 284 NGGLCCRQQFYIDFRLIGW-NDWIIAPAGYYGNYCEGSCPAYMAGVPGSASSFHTA

Query: 314 RQ-----CIASETASLPMIVSIKEGGRTRPQVVSLPNMRVQKCSA 35  
+ CI ++ +++ M+ E + V PNM V++C CA

Sbjct: 343 YMRGISPGSVNSCCIPTKLSTMSMLYFDDEYNIVKRDV---PNMIVEECGCA 39

tr Q9W6T9 Activin beta B protein (Fragment) [inhbb]  
Q9W6T9\_BRARE [Brachydanio rerio  
(Zebrafish) (Danio rerio)]

Score = 52.0 bits (123), Expect = 3e-05

Identities = 37/140 (26%), Positives = 62/140 (44%), Gaps = 25/140

Query: 231 GEPQLELHTLDLRDYGAQGDCDPEAPMTEGTRCCRQEMYIDLQGMKWAKNWVLEPP  
G QL+L L + G+ +CD G CCRQ+ YID + + W +W++ P

Sbjct: 1 GLEQLKLACLQVDSRSGFECGN----NGGLCCRQQFYIDFRLIGW-NDWIIAPA

Query: 291 YECVGTCQQ-----PPEALAFNWPFLGPRQ-----CIASETASLPMIVS

```
      C G+C      P A +F+  +  +      CI ++ +++ M+
Sbjct: 56 NYCEGSCPAYMAGVPGSASSFHTAVVNQYRMGMSPGSVNSCCIPTKLSTMSMLYF

Query: 334 GRTRPQVVSLPNMRVQKCSC 353
      + V   PNM V++C C
Sbjct: 116 NIVKRDV---PNMIVEECGC 132
```

```
tr   Q4AEG6      Bone morphogenetic protein 10 [Bmp10] [Rattus
      Q4AEG6_RAT  norvegicus (Rat)]

Score = 51.6 bits (122), Expect = 4e-05
Identities = 58/234 (24%), Positives = 89/234 (38%), Gaps = 51/234

Query: 107 LPPNSELVQAVLRLFQEPVPKAALHRHGRLSPRSAQARVTVEWLRVRDDGSN--RT
      +P + E+V A LRL+      L + RL      ++ + +   DGS   R+
Sbjct: 134 IPHHEEVVMAELRLY-----TLVQRDRMLYDGVDRKIIIFEVLESADGSEDEERS

Query: 165 SRLVSVH----ESGWKAFDVTEAVNFWXXXXXXXXXXXXXXXXXSVQREHL-----GPL
      LVS      S W+ FD+T+A   W      + ++      G L
Sbjct: 186 --LVSTEIYGTNSEWETFDITDATRRWQKSGPSTHQLEIHIESRQNQAEDTGRGQL

Query: 212 -ASGAHKLVRFASQGAPAGLGEPQLELHTL-----DLRDYGAQGDCDPEAPM--
      A H +      +G E + EL+ L      DL G G D EA +
Sbjct: 244 SAQNKHDPLLVVFSDDQSGDKEQKEELNELISHEQDLGLTDGFFGGPDEEALLQM

Query: 258 -----TEGTRCCRQEMYIDLQGMKWAKNWNVLEPPGFLAYECVGTCCQP 3
      +G C + +YID + + W +W++ PPG+ AYEC G C P
Sbjct: 304 IDDSTARIRRNAKGNKYCKKTPLYIDFKEIGW-DSWIIAPPGYEAYECRGVCNYP 3
```

```
tr   Q27W10      BMP5-8 (Fragment) [Nematostella vectensis]      3
      Q27W10_9CNID                                              a

Score = 51.6 bits (122), Expect = 4e-05
Identities = 41/161 (25%), Positives = 65/161 (40%), Gaps = 22/161

Query: 162 LIDSRLVSVHESGWKAFDVTEAVNFW-XXXXXXXXXXXXXXXXXSVQREHLGPLASG--
      LID R++ E GW+ FD++ A W      V+ + L P +G
Sbjct: 176 LIDQRVLRSWKEGWQEFDISAAGRVWSESPKKNYGLELSVVNFNNQELSPHLAGFV

Query: 215 -AHKLVRFASQGAPAGLGEPQLELHTLDLRDYGAQ-----GDCDPEAPMT
      K S G + E+H D+R + A      G DP A +
Sbjct: 236 LKEKRPFIVSFFKQDGEKKYTHEIHAHDIRQHRATRVSRSLPNAQVGGVDPR--S
```

Query: 263 CCRQEMYIDLQGMKWAKNWWLEPPGFLAYECVGTCQQPPEA 303  
C RQ +++ + ++W ++WV+ P G+ A+ C G C P A  
Sbjct: 294 CQRQALHVSFRKLRW-QDWVIAPEGYSAFYCSGECSFPLNA 333

tr Q589C7 Inhibin/activin beta B subunit (Fragment) [inhbb]  
Q589C7\_MESAU [Mesocricetus  
auratus (Golden hamster)]

Score = 51.2 bits (121), Expect = 6e-05  
Identities = 69/292 (23%), Positives = 116/292 (39%), Gaps = 47/29

Query: 81 SFREVAGRFLASEASTHLLVFGMEQRLPPNSELVQAVLRLFQEPVPKAALHRHGRL  
SF E G LAS S L F + N +VQA L L+ + +P  
Sbjct: 66 SFAETDG--LAS--SRVRLYFFVSNEGNQNLFVVQASLWLYLKLLPYVL-----

Query: 141 AQARVTVEWLRVRDDGSNRTSLIDSRLVSVHESGWKAFDVTEAVN-FWXXXXXXXXX  
++ +V V+ +R S+++ + V + SGW F +TEA+ +  
Sbjct: 114 SRRKVRVKVYYQEQQHGDRWSVVEKK-VDLKRSGWHTFPITEAIQALFERGERRLN

Query: 200 XVSVQREHLGPLASGAHKLVRFASQGAPAGLGEPQLELHTLDLRDYGAQGDCDPEA  
S Q + P+ + A LG+ + + L +CD  
Sbjct: 173 CDSCQELAVVPVFVDPGEESHRPFVVVQARLGDSRHRIRKRGL-----ECDGRT

Query: 260 GTRCCRQEMYIDLQGMKWAKNWWLEPPGFLAYECVGTCQQ-----PPEALAFNWPF  
CCRQ+ +ID + + W +W++ P G+ C G+C P A +F+  
Sbjct: 224 ---CCRQQFFIDFRLIGW-NDWIIAPTGYYGNYCEGSCPAYLAGVPGSASSFHTAV

Query: 312 -----GPRQ--CIASETASLPMIVSIKEGGTRTPQVVSLPNMRVQKCSA 354  
GP CI ++ +S+ M+ E + V PNM V++C CA  
Sbjct: 280 RMRGLNPGPVNSCCIPTKLSSMSMLYFDDEYNIVKRDV---PNMIVEECGCA 328

tr Q2LAG1 Activin beta B [Ctenopharyngodon idella (Grass  
Q2LAG1\_CTEID carp)]

Score = 50.8 bits (120), Expect = 7e-05  
Identities = 66/278 (23%), Positives = 106/278 (38%), Gaps = 71/27

Query: 110 NSELVQAVLRLFQEPVPKAALHRHGRLSPRSAQARVTVEWLRVRDDGSNRTSLIDS  
N ++QA L L+ + +P A + + +VTV G N +  
Sbjct: 153 NLYVLQANLWLYFKLLPGA-----QEKGLRRKVTVRVHYEYEPGGQNMHWPVME

Query: 170 VHESGWKAFDVTEAVNFWXXXXXXXXXXXXXXXXXSVQREHLGPLASGAHKLVRFASQG  
+ SGW F V+EAV RE L G + + +G

Sbjct: 205 LKRSGWHTFPVSEAV-----REMLAK--GGRRQDLDIHCEG

Query: 230 -----LGEPQLELHT--LDLRDYGAQG-----DCDPEAPMTEGTRCCRQEMY  
 L +P H L +R A+G +CD G CCRQ+ Y

Sbjct: 243 NVLPILVDPSDPSHRPFLVVRAQQAEGKHRIRKRGLECDGN----NGGLCCRQQFY

Query: 274 GMKWAKNWVLEPPGFLAYECVGTCQQ-----PPEALAFNWPFLGPRQ-----  
 + W +W++ P G+ C G+C P A +F+ + +

Sbjct: 299 LIGW-NDWIIAPAGYYGNYCEGSCPAYMAGVPGSASSFHTAVVNQYRMRGMSPGSV

Query: 317 IASETASLPMIVSIKEGGRTRPQVVSLPNMRVQKSCA 354  
 I ++ +++ M+ E + V PNM V++C CA

Sbjct: 358 IPTKLSTMSMLYFDDEYNIVKRDV---PNMIVEECGCA 392

tr Q4SES4 Chromosome 3 SCAF14614, whole genome shotgun  
 Q4SES4\_TETNG sequence  
 [GSTENG00019412001] [Tetraodon nigroviridis (Green  
 puffer)]

Score = 50.8 bits (120), Expect = 7e-05

Identities = 65/273 (23%), Positives = 104/273 (38%), Gaps = 63/27

Query: 110 NSELVQAVLRLRFQEPVPKAAALHRHGRLSPRSAQARVTVEWLRVRDDGSNRTSLIDS  
 N ++QA L L+ + +P A R R +VTV+ +R L++

Sbjct: 153 NLHVMQATLWLYFKVLPAPAEARSRR-----KVTVKVYYQEPGLGSRWDLVEK

Query: 170 VHESGWKAFDVTEAVNFWXXXXXXXXXXXXXXXXXSVQREHLGPLASGAHKLVRFASQG  
 + S W F +T+AV +R++L G ++G

Sbjct: 204 LKRSSWHTFVLTDVAVRLFQKGD-----RRQNLDVRCGECE-----AEG

Query: 230 LGEPQLELHTLDLRDYGAQGD-----CDPEAPMTEGTRCCRQEMYIDLQG  
 L + E H L Q D CD + + CCRQ+ YID +

Sbjct: 247 LLHQKDESHRPFLVVQARQADSKHRIRKRGLECDGSSSL-----CCRQQFYIDFRL

Query: 279 KNWVLEPPGFLAYECVGTCQQ-----PPEALAFNWPFL-----LGPRQ----CI  
 +W++ P G+ C G C P A +F+ +GP CI

Sbjct: 301 NDWIIAPSGYFGNYCEGNCPAYMPGVPGSASSFHTVVVNQYRLRGMGPGSMNSCCI

Query: 322 ASLPMIVSIKEGGRTRPQVVSLPNMRVQKSCA 354  
 +++ M+ E + V PNM V +C CA

Sbjct: 361 STMSMLYFDDEYNIVKRDV---PNMIVDECGCA 390

tr Q4VV68 Myostatin-II [gdf81] [Brachydanio rerio (Zebrafish) (Danio

Q4VV68\_BRARE rerio)]

Score = 50.4 bits (119), Expect = 1e-04

Identities = 59/249 (23%), Positives = 102/249 (40%), Gaps = 36/24

Query: 119 RLFQEPVPKAAALHRHGRLSPRSAQARVTVEWLRVRDDGSNRTSLIDSRL-VSVHES  
++ ++ KA L + R + ++ L +G+N ++ ++ V+

Sbjct: 141 KILPDSILKALLWIYLRPAEEPTTVYIQISHLESSEGNHNSRIRAQKIDVNARTD

Query: 178 FDVTEAVNFWXXXXXXXXXXXXXVSVQREHLGPLASGAHKLVRFASQGAPAGLGEP  
D+ ++ W S A+G V A G GL +P

Sbjct: 201 IDMKQLLKLWLKQPQSNFGIEIKASD-----ANGNDLAVTSAESGEE-GL-QP

Query: 238 HTLDL-----RDYGAQGDCDPEAPMTEGTRCCRQEMYIDLQGMKWAKNWWLEPPGF  
D RD G DCD + TE +RCCR + +D + W +W++ P +

Sbjct: 251 KISDTGKRSRRDTGL--DCDEHS--TE-SRCCRYPLTVDFEDFGW--DWIIPKRY

Query: 293 CVGTC-QQPPEALAFNWP----FLGPRQCIASETASLPMIVSIKEGGRTRPQVV--  
C G C Q+ P + N F GP CI ++ ++ M+ R Q++

Sbjct: 304 CSGECVQKYPHSHIVNKANPIFFAGP-CCILTKMSPINMLYF-----NDREQIIYG

Query: 346 MRVQKCSA 354

M V C C+

Sbjct: 358 MVVDLCGCS 366

sp 088959 Inhibin beta E chain precursor (Activin beta-E chain) 3  
INHBE\_RAT [Inhbe] 6  
[Rattus norvegicus (Rat)]

Score = 49.7 bits (117), Expect = 2e-04

Identities = 32/121 (26%), Positives = 53/121 (43%), Gaps = 27/121

Query: 251 CDPEAPMTEGTRCCRQEMYIDLQGMKWAKNWWLEPPGFLAYECVGTCQ-----QPP  
C+ E P+ CCR++ Y+D Q + W ++W+L+P G+ C G C P

Sbjct: 240 CESETPL-----CCRRDHYVDFQELGW-RDWILQPEGYQLNYCSGQCPPHLAGSPG

Query: 306 FN-----WPFLGPRQCIASETASLPMIVSIKEGGRTRPQVVSLPNMRVQ  
F+ WP G C+ + L ++ G + V P+M V+

Sbjct: 294 FHSAVFSLKANNPWP-AGSSCCVPTARRPLSLLYLDHNGNVVKTDV---PDMVVE

Query: 354 A 354

+

Sbjct: 350 S 350



```

sp . P17491          Inhibin beta B chain precursor (Activin beta-B chain) 4
    INHBB_RAT        [Inhbb]                                              2
                      [Rattus norvegicus (Rat)]

```

Score = 49.7 bits (117), Expect = 2e-04

Identities = 68/292 (23%), Positives = 116/292 (39%), Gaps = 47/29

```

Query: 81  SFREVAGRFLASEASTHLLVFGMEQRLPPNSELVQAVLRLFQEPVPKAAALHRHGRL
          SF E  G  LAS  S   L F +      N  +VQA L L+ + +P

```

```

Sbjct: 149 SFAETDG--LAS--SRVRLYFFVSNEGNQNLFVVQASLWLYLKLLPYVL-----

```

```

Query: 141 AQARVTVEWLRVRDDGSNRTSLIDSRLVSVHESGWKAFDVTEAVN-FWXXXXXXXXX
          ++ +V V+      +R ++++ + V +  SGW  F +TEA+  +

```

```

Sbjct: 197 SRRKVRVKVYFQEQGHGDRWNVVEKK-VDLKRSGWHTFPITEAIQALFERGERRLN

```

```

Query: 200 XSVSVQREHLGPLASGAHKLVRFASQGAPAGLGEPQLELHTLDRDYGAQGDCDPEA
          S Q   + P+      +      A LG+ + +  L      +CD

```

```

Sbjct: 256 CDSCQELAVVPVFVDPGEESHRRPFVVVQARLGDSRHRIRKRGL-----ECDGRT

```

```

Query: 260 GTRCCRQEMYIDLQGMKWAKNWVLEPPGFLAYECVGTCQQ-----PPEALAFNWP
          CCRQ+ +ID + + W  +W++ P G+      C G+C      P  A  +F+

```

```

Sbjct: 307 ---CCRQQFFIDFRLIGW-NDWIIAPTGYGYNYCEGSCPAYLAGVPGSASSFHTAV

```

```

Query: 312 -----GPRQ--CIASETASLPMIVSIKEGGRTRPQVVSLPNMRVQKCSA 354
          GP    CI ++ +S+ M+      E    +  V    PNM V++C CA

```

```

Sbjct: 363 RMRGLNPGPVNSCCIPTKLSSMSMLYFDDEYNIVKRDV---PNMIVEECGCA 411

```

```

sp   Q04999          Inhibin beta B chain precursor (Activin beta-B
    INHBB_MOUSE      chain) (Fragment)
                      [Inhbb] [Mus musculus (Mouse)]

```

Score = 49.7 bits (117), Expect = 2e-04

Identities = 68/292 (23%), Positives = 116/292 (39%), Gaps = 47/29

```

Query: 81  SFREVAGRFLASEASTHLLVFGMEQRLPPNSELVQAVLRLFQEPVPKAAALHRHGRL
          SF E  G  LAS  S   L F +      N  +VQA L L+ + +P

```

```

Sbjct: 105 SFAETDG--LAS--SRVRLYFFVSNEGNQNLFVVQASLWLYLKLLPYVL-----

```

```

Query: 141 AQARVTVEWLRVRDDGSNRTSLIDSRLVSVHESGWKAFDVTEAVN-FWXXXXXXXXX
          ++ +V V+      +R ++++ + V +  SGW  F +TEA+  +

```

```

Sbjct: 153 SRRKVRVKVYFQEQGHGDRWNVVEKK-VDLKRSGWHTFPITEAIQALFERGERRLN

```

```

Query: 200 XSVSVQREHLGPLASGAHKLVRFASQGAPAGLGEPQLELHTLDRDYGAQGDCDPEA
          S Q   + P+      +      A LG+ + +  L      +CD

```

```

Sbjct: 212 CDSCQELAVVPVFVDPGEESHRRPFVVVQARLGDSRHRIRKRGL-----ECDGRT

```

Query: 260 GTRCCRQEMYIDLQGMKWAKNWWLEPPGFLAYECVGTCCQ-----PPEALAFNWP  
CCRQ+ +ID + + W +W++ P G+ C G+C P A +F+  
Sbjct: 263 ---CCRQQFFIDFRLIGW-NDWIIAPTGYGNYCEGSCPAYLAGVPGSASSFHTAV  
  
Query: 312 -----GPRQ--CIASETASLPMIVSIKEGGRTRPQVVSLPNMRVQKSCA 354  
GP CI ++ +S+ M+ E + V PNM V++C CA  
Sbjct: 319 RMRGLNPGPVNSCCIPTKLSSMSMLYFDDEYNIVKRDV---PNMIVEECGCA 367

sp P27093 Inhibin beta B chain precursor (Activin beta-B :  
INHBB\_CHICK chain) [INHBB] :  
[Gallus gallus (Chicken)]

Score = 49.7 bits (117), Expect = 2e-04  
Identities = 56/251 (22%), Positives = 105/251 (41%), Gaps = 37/25

Query: 125 VPKAALHRHGRLSP----RSAQARVTVEWLRVRDDGSNRTSLIDSRLVSVHESGWK  
V +A+L + +L P + ++ +V V+ D SN+ ++++ + V + SGW  
Sbjct: 157 VVQASLWLYLKLLPYVLEKGSRRKVRVKVYFQDPDTSNKWNVVEKK-VDLKRSGWH

Query: 181 TEAVNFWXXXXXXXXXXXXXSVSVQREHLGPLASGAHKLVRFASQGAPAGLGEPQLE  
TEA+ + VQ E + + P + + +L  
Sbjct: 216 TEAIQ----ALFERGERRLNLDVQCEGCEEYSVLPIYVDPGEESHRPFLVVQARLA

Query: 241 DLRDYGAQGDCDPEAPMTEGTRCCRQEMYIDLQGMKWAKNWWLEPPGFLAYECVGT  
+R G + CD + CCRQ+ YID + + W +W++ P G+ C G+  
Sbjct: 272 RIRKRGLE--CDGRTNL-----CCRQQFYIDFRLIGW-NDWIIAPSGYYGNYCEGS

Query: 300 ----PPEALAFNWPFLGPRQ-----CIASETASLPMIVSIKEGGRTRPQ  
P A +F+ + + CI ++ +++ M+ E +  
Sbjct: 324 LAGVPGSASSFHTAVVNQYRMRGLNPGTVNSCCIPTKLSTMSMLYFDDEYNIVKRD

Query: 344 PNMVQKSCA 354  
PNM V++C CA  
Sbjct: 381 PNMIVEECGCA 391

tr Q3V1N0 15 days embryo head cDNA, RIKEN full-length enriched  
Q3V1N0\_MOUSE library,  
clone:4022431B02 product:inhibin beta-B, full insert  
sequence [Inhbb] [Mus musculus (Mouse)]

Score = 49.7 bits (117), Expect = 2e-04  
Identities = 68/292 (23%), Positives = 116/292 (39%), Gaps = 47/29

Query: 81 SFREVAGRFLASEASTHLLVFGMEQRLPPNSELVQAVLRLFQEPVPAALHRHGRL

```

          SF E G LAS S L F +      N +VQA L L+ + +P
Sbjct: 149 SFAETDG--LAS--SRVRLYFFVSNEGNQNLFFVQASLWLYLKLLPYVL-----

Query: 141 AQARVTVEWLRVRDDGSNRTSLIDSRLVSVHESGWKAFDVTEAVN-FWXXXXXXXXX
          ++ +V V+          +R ++++ + V + SGW F +TEA+ +
Sbjct: 197 SRRKVRVKVYFQEQQGHGDRWNVVEKK-VDLKRSGWHTFPITEAIQALFERGERRLN

Query: 200 XVSVQREHLGPLASGAHKLVRFASQGAPAGLGEPQLELHTLDLRDYGAQGD CDPEA
          S Q + P+ +          A LG+ + + L +CD
Sbjct: 256 CDSCQELAVVPFVDPGEESHRPFVVVQARLGDSRHRIRKRGL-----ECDGRT

Query: 260 GTRCCRQEMYIDLQGMKWAKNWWLEPPGFLAYECVGTCCQ-----PPEALAFNWPF
          CCRQ+ +ID + + W +W++ P G+ C G+C P A +F+
Sbjct: 307 ---CCRQQFFIDFRLIGW-NDWIIAPTGYGNYCEGSCPAYLAGVPGSASSFHTAV

Query: 312 -----GPRQ--CIASETASLPMIVSIKEGGRTRPQVVSLPNMRVQKCSCA 354
          GP CI ++ +S+ M+ E + V PNM V++C CA
Sbjct: 363 RMRGLNPGPVNSCCIPTKLSSMSMLYFDDEYNIVKRDV---PNMIVEECGCA 411

```

```

tr      Q1LYE4          Novel protein similar to vertebrate inhibin, alpha
      Q1LYE4_BRARE      (INHA)
                        [DKEY-91F15.2-001] [Brachydanio rerio (Zebrafish)
                        (Danio
                        rerio)]

```

Score = 49.3 bits (116), Expect = 2e-04

Identities = 28/100 (28%), Positives = 48/100 (48%), Gaps = 8/100

```

Query: 256 PMTEGTRCCRQEMYIDLQGMKWAKNWWLEPPGFLAYECVGTCCQPPEALAFNWPF
          P ++GT C R+++ I + + W NW++ P F Y C G C L
Sbjct: 253 PASQGTDCRREQIEISFEDLGW-NNWIVHPKSFTFYCHGNCSAERITT----IL

Query: 316 CIASETASLPMI--VSIKEGGRTRPQVVSLPNMRVQKCS 353
          C A S+ + + +GG + + +LPN+ ++C+C
Sbjct: 308 CCAPVPESMKS LRFTTTS DGGYSF-KYETLPNI IPEECNC 346

```

```

tr      Q90261          Activin beta B [inhbb] [Brachydanio rerio
      Q90261_BRARE      (Zebrafish) (Danio
                        rerio)]

```

Score = 49.3 bits (116), Expect = 2e-04

Identities = 59/249 (23%), Positives = 94/249 (37%), Gaps = 63/249

```

Query: 139 RSAQARVTVEWLRVRDDGSNRTSLIDSRLVSVHESGWKAFDVTEAVNFWXXXXXXXXX

```

```
      + +A+VTV          G N      + + V +   SGW   F V+EA+
Sbjct: 175 KGLRAKVTVRVHSYEPGGQNVHWPMM EKRV ELKRS GWHTFPVSEAI-----
Query: 199 XXVSVQREHLGPLASGAHKLVRFASQGAPAG-----LGEPQLELHT--LDLRDYGA
      RE L      G + +      +G A      L +P      H      L +R      A
Sbjct: 221 -----REMLAK--GRRQDLDIHCEGCEAANVLPILVDPSDPSHRPFLVVRAQQA
Query: 250 -----DCDPEAPMTEGTRCCRQEMYIDLQGMKWAKNWWLEPPGFLAYECVGTCQ
      +CD          G   CCRQ+ YID + + W   +W++ P G+      C G+C
Sbjct: 273 RIRKRGLECDGN----NGGLCCRQQFYIDFRLIGW-NDWIIAPAGYYGNYCEGSCP
Query: 300 --PPEALAFNWPFLGPRQ-----CIASETASLPMIVSIKEGGRTRPQVV
      P A +F+      +      +      CI ++ +++ M+      E      + V
Sbjct: 328 GVPGSASSFHTAVVNQYRMGMSPGSVNSCCIPTKLSTMSMLYFDDEYNIVKRDV-
Query: 346 MRVQKCSA 354
      M V++C CA
Sbjct: 385 MIVEECGA 393
```

```
sp P09529      Inhibin beta B chain precursor (Activin beta-B chain) [INHBB]
INHBB_HUMAN   [Homo
               sapiens (Human)]
```

Score = 48.5 bits (114), Expect = 4e-04

Identities = 66/292 (22%), Positives = 115/292 (39%), Gaps = 47/29

```
Query: 81  SFREVAGRFLASEASTHLLVFGMEQRLPPNSELVQAVLRLFQEPVPKAALHRHGRL
      SF E  G  LAS  S   L F +      N +VQA L L+ + +P
Sbjct: 145 SFAETDG--LAS--SRVRLYFFISNEGNQNLFVVQASLWLYLKLPLYVL-----
Query: 141 AQARVTVEWLRVRDDGSNRTSLIDSRLVSVHESGWKAFDVTEAVN-FWXXXXXXXXX
      ++ +V V+      +R ++++ R V +   SGW   F +TEA+      +
Sbjct: 193 SRRKVRVKVYFQEQQGHGDRWNMVEKR-VDLKRS GWHTFP LTEAIQALFERGERRLN
Query: 200 XSVSVQREHLGPLASGAHKLVRFASQGAPAGLGEPQLELHTLDLRDYGAQGDCEA
      S Q      + P+      +      A LG+ + +      L      +CD
Sbjct: 252 CDSCQELAVVPVFVDPGEESHRRPFVVVQARLGDSRHRIRKRG L-----ECDGRT
Query: 260 GTRCCRQEMYIDLQGMKWAKNWWLEPPGFLAYECVGTCQQ-----PPEALAFNWP
      CCRQ+ +ID + + W   +W++ P G+      C G+C      P A +F+
Sbjct: 303 ---CCRQQFFIDFRLIGW-NDWIIAPTGYGNYCEGSCPAYLAGVPGSASSFHTAV
Query: 315 Q-----CIASETASLPMIVSIKEGGRTRPQVVSLPNMRVQKCSA 354
      +      CI ++ +++ M+      E      + V   PNM V++C CA
Sbjct: 359 RMRGLNPGTVNSCCIPTKLSTMSMLYFDDEYNIVKRDV---PNMIVEECGA 407
```

tr Q53T31 Hypothetical protein INHBB [INHBB] [Homo sapiens  
Q53T31\_HUMAN (Human)]

Score = 48.5 bits (114), Expect = 4e-04

Identities = 66/292 (22%), Positives = 115/292 (39%), Gaps = 47/29

Query: 81 SFREVAGRFLASEASTHLLVFGMEQRLPPNSELVQAVLRLFQEPVPKAAALHRHGRL  
SF E G LAS S L F + N +VQA L L+ + +P  
Sbjct: 145 SFAETDG--LAS--SRVRLYFFISNEGNQNLFFVQASLWLYLKLLPYVL-----

Query: 141 AQARVTVEWLRVRDDGSNRTSLIDSRLVSVHESGWKAFDVTEAVN-FWXXXXXXXXX  
++ +V V+ +R ++++ R V + SGW F +TEA+ +  
Sbjct: 193 SRRKVRVKVYFQEQGHGDRWNMVEKR-VDLKRSGWHTFPLTEAIQALFERGERRLN

Query: 200 XVSVQREHLGPLASGAHKLVRFASQGAPAGLGEPQLELHTDLRDYGAQGDCDPEA  
S Q + P+ + A LG+ + + L +CD  
Sbjct: 252 CDSCQELAVVPVFVDPGEESHRRPFVVVQARLGDSRHRIRKRGL-----ECDGRT

Query: 260 GTRCCRQEMYIDLQGMKWAKNWWLEPPGFLAYECVGTCQ-----PPEALAFNWPF  
CCRQ+ +ID + + W +W++ P G+ C G+C P A +F+  
Sbjct: 303 ---CCRQQFFIDFRLIGW-NDWIIAPTGYGNYCEGSCPAYLAGVPGSASSFHTAV

Query: 315 Q-----CIASETASLPMIVSIKEGGRTRPQVVSLPNMRVQKCSA 354  
+ CI ++ +++ M+ E + V PNM V++C CA  
Sbjct: 359 RMRGLNPGTVNSCCIPTKLSTMSMLYFDDEYNIVKRDV---PNMIVEECGCA 407

sp P58166 Inhibin beta E chain precursor (Activin beta-E chain) [INHBE]  
INHBE\_HUMAN [Homo  
sapiens (Human)]

Score = 48.1 bits (113), Expect = 5e-04

Identities = 31/121 (25%), Positives = 52/121 (42%), Gaps = 27/121

Query: 251 CDPEAPMTEGTRCCRQEMYIDLQGMKWAKNWWLEPPGFLAYECVGTCQ-----QPP  
C+P P+ CCR++ Y+D Q + W ++W+L+P G+ C G C P  
Sbjct: 240 CEPATPL-----CCRRDHYVDFQELGW-RDWILQPEGYQLNYCSGQCPPHLAGSPG

Query: 306 FN-----WPFLGPRQCIASETASLPMIVSIKEGGRTRPQVVSLPNMRVQ  
F+ WP C+ + L ++ G + V P+M V+  
Sbjct: 294 FHSVAVFSLKANNPWP-ASTSCCVPTARRPLSLLYLDHNGNVVKTDV---PDMVVE

Query: 354 A 354

+  
Sbjct: 350 S 350

Database: UniProtKB

Posted date: Jun 13, 2006 4:15 PM  
Number of letters in database: 996,946,033  
Number of sequences in database: 3,053,606

Database: /home/local/blastnet/database/EXPASY//UniProtKB.01

Posted date: Jun 13, 2006 4:16 PM  
Number of letters in database: 53,383,733  
Number of sequences in database: 150,306

Lambda	K	H
0.322	0.136	0.436

Gapped

Lambda	K	H
0.267	0.0410	0.140

Matrix: BLOSUM62

Gap Penalties: Existence: 11, Extension: 1  
Number of Hits to DB: 717,696,099  
Number of Sequences: 3203912  
Number of extensions: 27249867  
Number of successful extensions: 50371  
Number of sequences better than 10.0: 100  
Number of HSP's better than 10.0 without gapping: 67  
Number of HSP's successfully gapped in prelim test: 587  
Number of HSP's that attempted gapping in prelim test: 49637  
Number of HSP's gapped (non-prelim): 883  
length of query: 366  
length of database: 1,050,329,766  
effective HSP length: 130  
effective length of query: 236  
effective length of database: 633,821,206  
effective search space: 149581804616  
effective search space used: 149581804616  
T: 11  
A: 40  
X1: 16 ( 7.4 bits)  
X2: 38 (14.6 bits)  
X3: 64 (24.7 bits)  
S1: 41 (21.9 bits)  
S2: 76 (33.9 bits)

Wallclock time: 9 seconds



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Molecular Genetics Laboratory  
Vancouver, Canada

Brett Casey, MD

Signature Genomic Laboratories

Spokane, WA

Lisa G Shaffer, PhD, FACMG; Bassem A Bejjani, MD,  
FACMG

Analysis of the entire  
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□ 1: J Clin Endocrinol Metab. 1993 May;76(5):1115-22.

[Related Articles, Links](#)

**Differential expression of messenger ribonucleic acids encoding insulin-like growth factors and their receptors in human uterine endometrium and decidua.**

**Giudice LC, Dsupin BA, Jin IH, Vu TH, Hoffman AR.**

Department of Gynecology and Obstetrics, Stanford University Medical Center, California 94305.

During the menstrual cycle, the endometrium undergoes characteristic changes in response to circulating sex steroids. Intense mitotic activity of glands and stroma occurs in the proliferative (estradiol-dominant) phase, and glandular secretion and stromal differentiation in the secretory (progesterone-dominant) phase. The insulin-like growth factors (IGF-I and IGF-II) promote cellular growth and differentiation and have been proposed to participate in these cyclic endometrial events, acting as mediators of steroid hormones. The objective of this study was to determine whether the messenger RNAs (mRNAs) encoding the IGF peptides and the type I and type II IGF receptors are differentially expressed in human endometrium during the menstrual cycle and in early pregnancy. A solution hybridization ribonuclease protection assay, using 32P-labeled riboprobes for IGF-I, IGF-II, and beta-actin (control), revealed IGF-I gene expression primarily in proliferative and early secretory endometrium and abundant IGF-II gene expression in mid-late secretory endometrium and early pregnancy decidua. Northern analysis, using IGF-I and IGF-II complementary DNA probes, revealed multiple IGF-I mRNAs [2-7.6 kilobase (kb)], expressed primarily in proliferative and early secretory endometrium, and IGF-II mRNAs (1.4-6.0 kb), expressed primarily in secretory endometrium and in early pregnancy decidua. The 7.6-kb IGF-I mRNA and the 6.0-kb IGF-II mRNA were most abundantly expressed. IGF-IEa and IGF-IEb mRNA splicing variants were present in a ratio of about 9:1, respectively. Type I and type II IGF receptor gene expression in endometrium was investigated using specific riboprobes and the ribonuclease protection assay. Messenger RNAs encoding both receptors were more abundantly expressed in the secretory phase and during early pregnancy, compared to the proliferative phase. These results show that mRNAs encoding the IGF peptides and their receptors are differentially expressed in human endometrium, depending on the steroid hormone milieu. The preferential expression of IGF-I mRNA in the proliferative phase supports the hypothesis that IGF-I is an estromedin in human endometrium. The expression of endometrial IGF-II mRNA in the mid to late secretory phase and in early pregnancy supports a role for IGF-II in differentiative functions of the endometrium, perhaps including endometrial tissue shedding in the menstrual cycle or remodeling during early pregnancy.

Set	Items	Description
S1	4	TGFB4
S2	8	TGF (N) BETA4
S3	218	TGF (N) (BETA (N) 4)
S4	154	EBAF?
S5	369	S1 OR S2 OR S3 OR S4
S6	359	S5 AND HUMAN?

? target s5/all

Your TARGET search request will retrieve up to 50 of the statistically most relevant records.

Searching ALL records

...Processing Complete

S7 19 TARGET - S5

Ending TARGET search. Enter TARGET to do another search in the present file(s), or BEGIN new file(s). Enter LOGOFF to disconnect from Dialog

? t s7/3,kwic/all

7/3,KWIC/1 (Item 1 from file: 654)

DIALOG(R)File 654:US Pat.Full.

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6551609 \*\*IMAGE Available

#### UTILITY

#### Method for diagnosing a pre-neoplastic or neoplastic lesion in transitional epithelial cells

Inventor: Tabibzadeh, Siamak, Albertson, NY, US

Assignee: Unassigned

Correspondence Address: Craig J. Arnold;Amster, Rothstein & Ebenstein, 90 Park Avenue, New York, NY, 10016, US

	Publication Number	Kind	Date	Application Number	Filing Date
Main Patent	US 20060099576	A1	20060511	US 200114320	20011211
Provisional				US 60-255641	20001214

Fulltext Word Count: 15258

#### Description of the Invention:

0109] The overexpression of **ebaf** in TCC of the bladder is presumably the consequence of genetic alterations, and is associated...greater sensitivity and specificity (Landman et al., 1998; and Ramakumar et al., 1999). Quantification of **ebaf** also may be a useful biomarker for screening for TCC of the bladder, and potentially...of the bladder tumors used in this study, in accordance with this classification, revealed that **ebaf** was detected at a low level in the urine of patients with hyperplasia, but that...

...In the majority of patients who had low-grade papillary transitional-cell carcinoma, amounts of **ebaf** found in the urine were lower than the amounts of **ebaf** found in the urine of patients with high-grade carcinomas. These findings show that the overexpression of **ebaf** correlates with the degree of morphologic differentiation of transitional-cell carcinomas, with those having a poor prognosis showing the potential to secrete more **ebaf** into the urine0124] 12. Kothapalli et al., Detection of **ebaf**, a novel human gene of the TGF-[small beta, Greek] superfamily; association of gene expression...0142] 32. Tabibzadeh et al., Distinct tumor specific expression of **TGFB4** (**ebaf**), a novel human gene of the TGF-beta superfamily. Front. Biosci.,

2:a18-25, 1997...

7/3,KWIC/2 (Item 2 from file: 654)

DIALOG(R)File 654:US Pat.Full.

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6526950

Derwent Accession: 2004-212616

**UTILITY**

**Secreted and transmembrane polypeptides and nucleic acids encoding the same**

Inventor: Goddard, Audrey, San Francisco, CA, US

Godowski, Paul J., Burlingame, CA, US

Gurney, Austin L., Belmont, CA, US

Roy, Margaret Ann, San Francisco, CA, US

Wood, William I., Hillsborough, CA, US

Assignee: Genetech, Inc., (02), South San Francisco, CA, US

Examiner: Kemmerer, Elizabeth C.

Legal Representative: Heller Ehram LLP

	Publication Number	Kind	Date	Application Number	Filing Date
	-----	--	-----	-----	-----
Main Patent	US 7033825	B2	20060425	US 2001907841	20010717
Related Publ	US 20020198366	A1	20021226		
Continuation	PENDING			US 2000665350	20000918
Continuation	PENDING			WO 2000US4414	20000222
CIP	PENDING			WO 2000US3565	20000211
CIP	PENDING			WO 98US19330	19980916
Provisional				US 60-63045	19971024

US Term Extension: 13 days

Fulltext Word Count: 110201

**Summary of the Invention:**

...related proteins and which are necessary for the formation of the cysteine knot structure. The **EBAF** sequence contains an additional cysteine residue, 12 amino acids upstream from the first conserved cysteine...

...contain an additional cysteine residue are TGF-[small beta, Greek]s, inhibins, and GDF-3. **EBAF**, similar to LEFTY, GDF-3/Vgr2, and GDF-9, lacks the cysteine residue that is known to form the intermolecular disulfide bond. Therefore, **EBAF** appears to be an additional member of the TGF-[small beta, Greek] superfamily with an...

...the two monomer subunits may promote dimer formation. Fluorescence in situ hybridization showed that the **ebaf** gene is located on human chromosome 1 at band q42.1...

...0100] Additional members of the TGF-[small beta, Greek] superfamily, such as those related to **EBAF**, are being searched for by industry and academics. We herein describe the identification and characterization of novel polypeptides having homology to **EBAF**, designated herein as PRO317 polypeptides...

7/3,KWIC/3 (Item 3 from file: 654)

DIALOG(R)File 654:US Pat.Full.

(c) Format only 2006 Dialog. All rts. reserv.

6363457 \*\*IMAGE Available  
Derwent Accession: 2005-725765

**UTILITY**

**Humanized anti-TGF-beta antibodies**

Inventor: Adams, Camellia W., San Jose, CA, US  
Ferrara, Napoleone, San Francisco, CA, US  
Filvaroff, Ellen H., San Francisco, CA, US  
Mao, Weiguang, San Mateo, CA, US  
Presta, Leonard G., San Francisco, CA, US  
Tejada, Max L., Campbell, CA, US

Assignee: Genentech, Inc., (02), South San Francisco, CA, US

Correspondence Address: GENENTECH, INC., 1 DNA WAY, SOUTH SAN FRANCISCO, CA  
94080, US

	Publication Number	Kind	Date	Application Number	Filing Date
	-----	--	-----	-----	-----
Main Patent	US 20050276802	A1	20051215	US 200596046	20050331
Provisional				US 60-558290	20040331

Fulltext Word Count: 39570

**Description of the Invention:**

...to any one of the currently identified forms, including TGF-beta1, TGF-beta2, TGF-beta3, **TGF - beta4**, and TGF-beta5 and latent versions thereof, as well as to human TGF-beta species...

...the sequence. The specific terms "TGF-beta1," "TGF-beta2," and "TGF-beta3", as well as " **TGF - beta4** " and "TGF-beta5," refer to the TGF-betas defined in the literature, e.g., Derynck...

**7/3,KWIC/4 (Item 4 from file: 654)**

DIALOG(R)File 654:US Pat.Full.

(c) Format only 2006 Dialog. All rts. reserv.

6611218

**UTILITY**

**IgG immunoglobulin variants with optimized effector function**

Inventor: Lazar, Gregory Alan, Los Angeles, CA, US  
Dahiyat, Bassil I., Altadena, CA, US  
Dang, Wei, Pasadena, CA, US  
Karki, Sher Bahadur, Pomona, CA, US  
Vafa, Omid, Monrovia, CA, US

Assignee: Xencor, Inc., (02)

Correspondence Address: DORSEY & WHITNEY LLP, 555 CALIFORNIA STREET, SUITE  
1000, SUITE 1000, SAN FRANCISCO, CA, 94104, US

	Publication Number	Kind	Date	Application Number	Filing Date
	-----	--	-----	-----	-----
Main Patent	US 20060134105	A1	20060622	US 2005256060	20051021
Provisional				US 60-621387	20041021
Provisional				US 60-629068	20041118
Provisional				US 60-652968	20050214
Provisional				US 60-659004	20050303

Fulltext Word Count: 68454

**Description of the Invention:**

...beta RII, TGF-beta RIIB, TGF-beta RIII, TGF-beta1, TGF-beta2, TGF-beta3, TGF- **beta4** , TGF -beta5, Thrombin, Thymus Ck-1,

7/3,KWIC/5 (Item 5 from file: 654)  
DIALOG(R)File 654:US Pat.Full.  
(c) Format only 2006 Dialog. All rts. reserv.

6602289

**UTILITY**

**Povidone-containing carriers for polypeptide growth factors**

Inventor: Akella, Rama, Austin, TX, US

Ranieri, John, Atlanta, GA, US

Assignee: Zimmer Orthobiologics, Inc., (02)

Correspondence Address: WILLIAMS, MORGAN & AMERSON, 10333 RICHMOND, SUITE 1100, HOUSTON, TX, 77042, US

	Publication Number	Kind	Date	Application Number	Filing Date
	-----	--	-----	-----	-----
Main Patent	US 20060128625	A1	20060615	US 2006338914	20060125
Division	US 6992066			US 200127669	20011221
CIP	PENDING			US 2000748038	20001222
CIP	US 6211157			US 98173989	19981016

Fulltext Word Count: 7520

Description of the Invention:

...13, BMP-14, BMP-15, TGF-beta-1, TGF-beta-2, TGF-beta-3, TGF- **beta** - 4 ; and TGF-beta-5; growth/differentiation factors such as GDF-1, GDF-3, GDF-5...

7/3,KWIC/6 (Item 6 from file: 654)  
DIALOG(R)File 654:US Pat.Full.  
(c) Format only 2006 Dialog. All rts. reserv.

6590888

**UTILITY**

**Production of TNFR-lg**

Inventor: Drapeau, Denis, Salem, NH, US

Luan, Yen-Tung, Chelmsford, MA, US

Mercer, James R., Derry, NH, US

Wang, Wenge, North Chelmsford, MA, US

Lasko, Daniel R., Medford, MA, US

Assignee: Wyeth Research Ireland Limited, (02), Newbridge, IE

Correspondence Address: CHOATE, HALL & STEWART LLP, PATENT GROUP, TWO INTERNATIONAL PLACE, BOSTON, MA, 02110, US

	Publication Number	Kind	Date	Application Number	Filing Date
	-----	--	-----	-----	-----
Main Patent	US 20060121569	A1	20060608	US 2005213633	20050825
Provisional				US 60-605379	20040827

Fulltext Word Count: 29999

Description of the Invention:

...alpha and TGF-beta, including TGF-beta 1, TGF-beta 2, TGF-beta 3,

TGF- **beta** 4 , or TGF-beta 5; insulin-like growth factor-I and -II  
(IGF-I and IGF...

7/3,KWIC/7 (Item 7 from file: 654)  
DIALOG(R)File 654:US Pat.Full.  
(c) Format only 2006 Dialog. All rts. reserv.

6590887

**UTILITY**

**Production of polypeptides**

Inventor: Drapeau, Denis, Salem, NH, US  
Luan, Yen-Tung, Chelmsford, MA, US  
Mercer, James R., Derry, NH, US  
Wang, Wenge, North Chelmsford, MA, US  
Lasko, Daniel R., Medford, MA, US  
Assignee: Wyeth Research Ireland Limited, (02), Newbridge, IE  
Correspondence Address: CHOATE, HALL & STEWART LLP, PATENT GROUP, TWO  
INTERNATIONAL PLACE, BOSTON, MA, 02110, US

	Publication Number	Kind	Date	Application Number	Filing Date
	-----	--	-----	-----	-----
Main Patent	US 20060121568	A1	20060608	US 2005213308	20050825
Provisional				US 60-605097	20040827
Provisional				US 60-604941	20040827
Provisional				US 60-605074	20040827

Fulltext Word Count: 30049

Description of the Invention:

...alpha and TGF-beta, including TGF-beta 1, TGF-beta 2, TGF-beta 3,  
TGF- **beta** 4 , or TGF-beta 5; insulin-like growth factor-I and -II  
(IGF-I and IGF...

7/3,KWIC/8 (Item 8 from file: 654)  
DIALOG(R)File 654:US Pat.Full.  
(c) Format only 2006 Dialog. All rts. reserv.

6572043

**UTILITY**

**Compound having tgf[sharp s, German (sz ligature)] inhibitory activity and medicinal composition containing the same**

Inventor: Shimizu, Kiyoshi, Gunma-Ken, JP  
Shimizu, Toshiyuki, Gunma-Ken, JP  
Kimura, Kaname, Gunma-Ken, JP  
Kawakami, Kazuki, Gunma-Ken, JP  
Nakoji, Masayoshi, Gunma-Ken, JP  
Assignee: Kirin Beer Kabushiki Kaisha, (03), 10-1, Shinkawa 2-chome,  
Chuo-ku, Tokyo, 104-8288, JP  
Correspondence Address: OBLON, SPIVAK, MCCLELLAND, MAIER & NEUSTADT, P.C.,  
1940 DUKE STREET, ALEXANDRIA, VA, 22314, US

	Publication Number	Kind	Date	Application Number	Filing Date
	-----	--	-----	-----	-----
Main Patent	US 20060111375	A1	20060525	US 2003525087	20030822
PCT	WO 2003JP10647		20030822		
Priority				JP 2002244028	20020823

Fulltext Word Count: 161571

Description of the Invention:

...0731] The term "TGF[small **beta** , Greek] inhibitory activity" as used herein means that the compound has the activity of inhibition...

7/3,KWIC/9 (Item 9 from file: 654)

DIALOG(R)File 654:US Pat.Full.

(c) Format only 2006 Dialog. All rts. reserv.

6466327

Derwent Accession: 2006-238200

**UTILITY**

**Microorganisms for therapy**

Inventor: Szalay, Aladar A., Highland, CA, US  
Timiryasova, Tatyana, Scotrun, PA, US  
Yu, Yong A., San Diego, CA, US  
Zhang, Qian, San Diego, CA, US

Assignee: Unassigned

Correspondence Address: FISH & RICHARDSON, PC, P.O. BOX 1022, MINNEAPOLIS, MN, 55440-1022, US

	Publication Number	Kind	Date	Application Number	Filing Date
	-----	--	-----	-----	-----
Main Patent	US 20060051370	A1	20060309	US 2005238025	20050927
Continuation	PENDING			US 2004872156	20040618
Priority				EP 200313826	20030618
				EP 200318478	20030814
				EP 200324283	20031022

Fulltext Word Count: 66883

Description of the Invention:

...e4f, e4fl, e4tfla, e4tflb, eal, eaacl, eaatl, eaat2, eac, ead, eag, eap, earl, ear2, ear3, **ebaf** , ebf, ebl, ebm, ebnl, ebnl, ebn2, ebr2a, ebsl, ebvml, ebvsl, ecl, ecal, ecb2, ecel, ecgfl...tfpi, tfpi2, tfr, tfrc, tfsl, tft, tg, tg737, tgb1, tgb2, tgd, tgfa, tgfb1, tgfb2, tgfb3, **tgfb4** , tgfb1, tgfb1, tgfb2, tgfb3, tgfbre, tgfr, tgm1, tgm2, tgm3, tgm4, tgn38, tgn46, th, thas, thbd...

7/3,KWIC/10 (Item 10 from file: 654)

DIALOG(R)File 654:US Pat.Full.

(c) Format only 2006 Dialog. All rts. reserv.

6428948 \*\*IMAGE Available

Derwent Accession: 2006-135882

**UTILITY**

**Compositions and methods for production of disulfide bond containing proteins in host cells**

Inventor: Beckwith, Jonathan, Cambridge, MA, US  
Aslund, Fredrik, Stockholm, SE  
Bessette, Paul H., Camarillo, CA, US  
Georgiou, George, Austin, TX, US  
Ritz, Daniel, Everett, MA, US  
Lim, Jackie Eun-ah, Shrewsbury, MA, US

Assignee: Unassigned

Correspondence Address: FOLEY HOAG, LLP;PATENT GROUP, WORLD TRADE CENTER  
WEST, 155 SEAPORT BLVD, BOSTON, MA, 02110, US

	Publication Number	Kind	Date	Application Number	Filing Date
Main Patent	US 20060030022	A1	20060209	US 200558926	20050216
Continuation	US 6872563			US 2000679705	20001005
Provisional				US 60-157770	19991005
Provisional				US 60-163939	19991108
Provisional				US 60-166044	19991117

Fulltext Word Count: 28817

Description of the Invention:

...alpha and TGF-beta, including TGF-beta 1, TGF-beta 2, TGF-beta 3,  
TGF- **beta 4** , or TGF-beta 5; insulin-like growth factor-I and -II  
(IGF-I and IGF...

7/3,KWIC/11 (Item 11 from file: 654)

DIALOG(R)File 654:US Pat.Full.

(c) Format only 2006 Dialog. All rts. reserv.

6419661 \*\*IMAGE Available

Derwent Accession: 2006-117602

**UTILITY**

**Optimized Fc variants**

Inventor: Lazar, Gregory Alan, Los Angeles, CA, US

Dang, Wei, Pasadena, CA, US

Desjarlais, John J., Pasadena, CA, US

Karki, Sher Bahadur, Pasadena, CA, US

Vafa, Omid, Monrovia, CA, US

Hayes, Robert, Paoli, PA, US

Assignee: Xencor, Inc., (02), Monrovia, CA, US

Correspondence Address: DORSEY & WHITNEY LLP, 555 CALIFORNIA STREET, SUITE  
1000, SUITE 1000, SAN FRANCISCO, CA, 94104, US

	Publication Number	Kind	Date	Application Number	Filing Date
Main Patent	US 20060024298	A1	20060202	US 2005124620	20050505
CIP	PENDING			US 2004822231	20040326
CIP	PENDING			US 2003672280	20030926
CIP	PENDING			US 2003379392	20030303

Fulltext Word Count: 58874

Description of the Invention:

...beta RII, TGF-beta RIIB, TGF-beta RIII, TGF-beta1, TGF-beta2,  
TGF-beta3, TGF- **beta4** , TGF -beta5, Thrombin, Thymus Ck-1, Thyroid  
stimulating hormone, Tie, TIMP, TIQ, Tissue Factor, TMEFF2, Tmpo...

7/3,KWIC/12 (Item 12 from file: 654)

DIALOG(R)File 654:US Pat.Full.

(c) Format only 2006 Dialog. All rts. reserv.

6414745



Derwent Accession: 2003-625378

**UTILITY**

**Povidone-containing carriers for polypeptide growth factors**

Inventor: Akella, Rama, Austin, TX, US

Ranieri, John, Atlanta, GA, US

Assignee: Zimmer Orthobiologics, Inc., (02), Austin, TX, US

Examiner: Russel, Jeffrey Edwin

Legal Representative: Williams, Morgan & Amerson, P.C.

	Publication Number	Kind	Date	Application Number	Filing Date
Main Patent	US 6992066	B2	20060131	US 200127669	20011221
Related Publ	US 20030022828	A1	20030130		
CIP	PENDING			US 2000748038	20001222
CIP	US 6211157	A		US 98173989	19981016

US Term Extension: 153 days

Fulltext Word Count: 8238

Summary of the Invention:

...13, BMP-14, BMP-15, TGF-beta-1, TGF-beta-2, TGF-beta-3, TGF- **beta** -  
4 , and TGF-beta-5; growth/differentiation factors such as GDF-1, GDF-3,  
GDF-5...

**7/3,KWIC/13 (Item 13 from file: 654)**

DIALOG(R)File 654:US Pat.Full.

(c) Format only 2006 Dialog. All rts. reserv.

6396610

Derwent Accession: 2006-088707

**UTILITY**

**Novel 27875, 22025, 27420, 17906, 16319, 55092 and 10218 molecules and uses therefor**

Inventor: Kapeller-Libermann, Rosana, Chestnut Hill, MA, US

White, David, Braintree, MA, US

Robison, Keith E., Wilmington, MA, US

MacBeth, Kyle J., Boston, MA, US

Carroll, Joseph M., Cambridge, MA, US

Cook, William James, Hanover, NH, US

Meyers, Rachel E., Newton, MA, US

Chun, Miyoung, Belmont, MA, US

Williamson, Mark J., Saugus, MA, US

Assignee: Millennium Pharmaceuticals, Inc., (02)

Correspondence Address: MILLENNIUM PHARMACEUTICALS, INC., 40 Landsdowne  
Street, CAMBRIDGE, MA, 02139, US

	Publication Number	Kind	Date	Application Number	Filing Date
Main Patent	US 20060009632	A1	20060112	US 2005226701	20050914
Division	PENDING			US 2003386414	20030311
Division	US 6146876			US 99330970	19990611
Division	ABANDONED			US 2000571689	20000516
CIP	ABANDONED			US 99426282	19991025
CIP	ABANDONED			US 2000668266	20000922
CIP	ABANDONED			US 2000724599	20001128
CIP	ABANDONED			US 2001860193	20010516
CIP	PENDING			US 2002283023	20021029

CIP	ABANDONED	US 200110943	20011206
CIP	ABANDONED	US 2001833082	20010410
Provisional		US 60-335044	20011031
Provisional		US 60-254037	20001207

Fulltext Word Count: 231802

**7/3,KWIC/14 (Item 14 from file: 654)**  
 DIALOG(R)File 654:US Pat.Full.  
 (c) Format only 2006 Dialog. All rts. reserv.

6395854  
 Derwent Accession: 2006-070918

**UTILITY**

**ME-5, ME-2, and EPP2: human protein antigens reactive with autoantibodies present in the serum of women suffering from endometriosis**

Inventor: Shami, A. Said El, Camarillo, CA, US  
 Campbell, Bruce, Calabasas, CA, US  
 Sustarsic, Dennis, Seal Beach, CA, US  
 Sahakian, Niver, Encino, CA, US

Assignee: Unassigned

Correspondence Address: JOSEPH E. MUETH, ESQ., 8TH FLOOR, 225 SOUTH LAKE AVE., PASADENA, CA, 91101, US

	Publication Number	Kind	Date	Application Number	Filing Date
	-----	--	-----	-----	-----
Main Patent	US 20060008876	A1	20060112	US 2004887540	20040707

Fulltext Word Count: 19246

Summary of the Invention:

...protease cathepsin S in a clinical sample. A gene encoding an endometrial bleeding associated factor ( **ebaf** ) is described in U.S. Pat. No. 6,294,662 and this gene could be useful for diagnosis of endometriosis. However the **ebaf** gene seems to have better utility in the early diagnosis of selected carcinomas (colon, ovaries...

**7/3,KWIC/15 (Item 15 from file: 654)**  
 DIALOG(R)File 654:US Pat.Full.  
 (c) Format only 2006 Dialog. All rts. reserv.

6523820  
 Derwent Accession: 2006-327603

**UTILITY**

**Human cDNA clones comprising polynucleotides encoding polypeptides and methods of their use**

Inventor: Williams, Lewis T., Mill Valley, CA, US  
 Chu, Keting, Woodside, CA, US  
 Lee, Ernestine, Kensington, CA, US  
 Hestir, Kevin, Kensington, CA, US  
 Wong, Justin, Oakland, CA, US  
 Doberstein, Stephen K., San Francisco, CA, US

Assignee: Unassigned

Correspondence Address: FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER;LLP, 901 NEW YORK AVENUE, NW, WASHINGTON, DC, 20001-4413, US

	Publication Number	Kind	Date	Application Number	Filing Date
Main Patent	US 20060084799	A1	20060420	US 2004948571	20040924
Provisional				US 60-505144	20030924
Provisional				US 60-548191	20040301
Provisional				US 60-589826	20040722
Provisional				US 60-589788	20040722

Fulltext Word Count: 62323

7/3,KWIC/16 (Item 16 from file: 654)  
 DIALOG(R)File 654:US Pat.Full.  
 (c) Format only 2006 Dialog. All rts. reserv.

6522739 \*\*IMAGE Available  
 Derwent Accession: 2006-253503

#### UTILITY

#### Novel therapy for lysosomal enzyme deficiencies

Inventor: Ginns, Edward I., Shewsbury, MA, US

Ostroff, Gary R., Worcester, MA, US

Assignee: University of Massachusetts, (02), Boston, MA, US

Correspondence Address: GODFREY & KAHN S.C., 780 NORTH WATER STREET,  
 MILWAUKEE, WI, 53202, US

	Publication Number	Kind	Date	Application Number	Filing Date
Main Patent	US 20060083718	A1	20060420	US 2005230017	20050919
CIP	PENDING			US 2004869693	20040616
Provisional				US 60-610872	20040917

Fulltext Word Count: 35039

#### Description of the Invention:

...such as TGF-alpha and TGF-beta, including TGF-beta1, TGF-beta2,  
 TGF-beta3, TGF- **beta4** , or TGF-beta5; insulin-like growth factor-I and  
 -II (IGF-I and IGF-II...

7/3,KWIC/17 (Item 17 from file: 654)  
 DIALOG(R)File 654:US Pat.Full.  
 (c) Format only 2006 Dialog. All rts. reserv.

6513713 \*\*IMAGE Available  
 Derwent Accession: 2005-163229

#### UTILITY

#### Gene expression profiling in primary ovarian serous papillary tumors and normal ovarian epithelium

Inventor: Santin, Alessandro D., Little Rock, AR, US

Assignee: Unassigned

Correspondence Address: Benjamin Aaron Adler;ADLER & ASSOCIATES, 8011  
 Candle Lane, Houston, TX, 77071, US

	Publication Number	Kind	Date	Application Number	Filing Date
Main Patent	US 20060078941	A1	20060413	US 2005298777	20051209

CIP  
Provisional

PENDING

US 2004862517 20040607  
US 60-476934 20030609

Fulltext Word Count: 10667

Exemplary or Independent Claim(s):

...TGFB3, SPARCL1, ALDH1A1, TM4SF3, ABCA8, RNASE4, ITM2A, NR1H4,  
PLA2G2A, APOD, CHL1, SEPP1, IGF1, SEMACAP3, GPM6A, **EBAF**, GSTM5,  
COL14A1, VWF, AOX1, MAF, PIPPIN, NR4A1, COL15A1, SFRP4, MFAP4,  
PDGFRA, GATM, STAR, LAMA2, FABP4...

7/3,KWIC/18 (Item 18 from file: 654)

DIALOG(R)File 654:US Pat.Full.

(c) Format only 2006 Dialog. All rts. reserv.

6410699

Derwent Accession: 2005-533851

**UTILITY**

**Design of therapeutics and therapeutics**

Inventor: Ault-Riche, Dana, Los Gatos, CA, US

Levy, Ronald, Stanford, CA, US

Assignee: Unassigned

Correspondence Address: FISH & RICHARDSON, PC, P.O. BOX 1022, MINNEAPOLIS,  
MN, 55440-1022, US

	Publication Number	Kind	Date	Application Number	Filing Date
	-----	--	-----	-----	-----
Main Patent	US 20060018911	A1	20060126	US 200532773	20050110
Provisional				US 60-557591	20040329
Provisional				US 60-536184	20040112

Fulltext Word Count: 60177

Description of the Invention:

...Greek], e.g., activins, bone morphogenic proteins (BMPs) and  
receptors (BMPRs), endometrial bleeding associated factor ( **EBAF** ),  
inhibin A and MIC-1); transforming growth factors alpha (TGFs-[small  
alpha, Greek]); insulin-like...

7/3,KWIC/19 (Item 19 from file: 654)

DIALOG(R)File 654:US Pat.Full.

(c) Format only 2006 Dialog. All rts. reserv.

6370944 \*\*IMAGE Available

Derwent Accession: 2006-115511

**UTILITY**

**Drug delivery product and methods**

Inventor: Ostroff, Gary R., Worcester, MA, US

Assignee: Unassigned

Correspondence Address: GODFREY & KAHN S.C., 780 NORTH WATER STREET,  
MILWAUKEE, WI, 53202, US

	Publication Number	Kind	Date	Application Number	Filing Date
	-----	--	-----	-----	-----
Main Patent	US 20050281781	A1	20051222	US 2004869693	20040616

Fulltext Word Count: 32658

Description of the Invention:

...such as TGF-alpha and TGF-beta, including TGF-beta1, TGF-beta2, TGF-beta3, TGF- **beta4** , or TGF-beta5; insulin-like growth factor-I and -II (IGF-I and IGF-II...

? logoff hold

```
23jun06 14:15:28 User228206 Session D2614.12
    $0.53      0.074 DialUnits File652
$0.53 Estimated cost File652
    $33.99      5.761 DialUnits File654
        $13.30  19 Type(s) in Format  3
        $9.50  38 Type(s) in Format  6
    $22.80  57 Types
$56.79 Estimated cost File654
        OneSearch, 2 files,  5.835 DialUnits FileOS
    $1.06 TELNET
$58.38 Estimated cost this search
$75.68 Estimated total session cost   8.184 DialUnits
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Logoff: level 05.12.03 D 14:15:28

You are now logged off

? t s5/6,kwic/all  
>>>KWIC option is not available in file(s): 399

**5/6,KWIC/1 (Item 1 from file: 73)**  
DIALOG(R)File 73:(c) 2006 Elsevier Science B.V. All rts. reserv.

06761297 EMBASE No: 1997042786  
**Transforming growth factor beta in diabetic nephropathy**  
1996

DRUG TERMS (UNCONTROLLED): transforming growth factor beta antagonist  
--pharmacology--pd; **transforming growth factor beta antibody**  
--pharmacology--pd

**5/6,KWIC/2 (Item 2 from file: 73)**  
DIALOG(R)File 73:(c) 2006 Elsevier Science B.V. All rts. reserv.

06717049 EMBASE No: 1996190191  
**Marked diversity in the action of growth factors on**  
**N-methyl-D-aspartate-induced neuronal degeneration**  
1996

...DRUG TERMS (UNCONTROLLED): brain derived neurotrophic factor--drug  
toxicity--to; recombinant brain derived neurotrophic factor--drug  
comparison--cm; **transforming growth factor beta antibody** --pharmacology  
--pd; **transforming growth factor beta antibody** --drug interaction--it

**5/6,KWIC/3 (Item 3 from file: 73)**  
DIALOG(R)File 73:(c) 2006 Elsevier Science B.V. All rts. reserv.

06421169 EMBASE No: 1996077869  
**Transforming growth factor-beta in in vivo resistance**  
1996

DRUG TERMS (UNCONTROLLED): **transforming growth factor beta antibody** --drug  
toxicity--to; **transforming growth factor beta antibody** --pharmacology--pd;  
**transforming growth factor beta antibody** --drug therapy--dt; **transforming**  
**growth factor beta antibody** --drug dose--do

**5/6,KWIC/4 (Item 4 from file: 73)**  
DIALOG(R)File 73:(c) 2006 Elsevier Science B.V. All rts. reserv.

06350226 EMBASE No: 1996003775  
**Anti-(transforming growth factor beta) antibodies with predefined**  
**specificity inhibit metastasis of highly tumorigenic human xenotransplants**  
**in nu/nu mice**  
1995

DRUG TERMS (UNCONTROLLED): **transforming growth factor beta antibody**  
--pharmacology--pd; **transforming growth factor beta antibody** --drug  
development--dv; **transforming growth factor beta antibody** --drug dose--do

**5/6,KWIC/5 (Item 5 from file: 73)**  
DIALOG(R)File 73:(c) 2006 Elsevier Science B.V. All rts. reserv.

06155894 EMBASE No: 1995181304

**Perspectives in the treatment of liver fibrosis**  
1995

DRUG TERMS (UNCONTROLLED): s 0885--pharmacology--pd; s 0885--drug therapy  
--dt; **transforming growth factor beta antibody** --pharmacology--pd

**5/6,KWIC/6 (Item 6 from file: 73)**

DIALOG(R)File 73:(c) 2006 Elsevier Science B.V. All rts. reserv.

06046762 EMBASE No: 1995077061

**Expression of tissue-type plasminogen activator and its inhibitor couples  
with development of capillary network by human microvascular endothelial  
cells on matrigel**  
1995

et	Items	Description
S1	21	'TGFB4'
S2	263	'TRANSFORMING GROWTH FACTOR BETA ANTIBODY'
S3	246	S2/1997:2006
S4	17	S2 NOT S3
S5	17	RD (unique items)
S6	125	E1-E8
S7	15	'TRANSFORMING GROWTH FACTOR BETA CDNA' OR E20-E26
S8	6	E13-E16
S9	3	'TRANSFORMING GROWTH FACTOR BETA NEUTRALIZING A'
S10	36	E2-E6
S11	3	'TRANSFORMING GROWTH FACTOR BETA 1 ANTIBODY'
S12	5	E34-E36
S13	1	'TRANSFORMING GROWTH FACTOR BETA 4 GENE'
S14	2	E39-E40
S15	18	'TRANSFORMING GROWTH FACTOR BETA4'
S16	1	'TRANSFORMING GROWTH FACTOR B4'
S17	215	S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16
S18	201	S17/1997:2006

? s s17 not s18

215 S17

201 S18

S19 14 S17 NOT S18

? s s19 or s4

14 S19

17 S4

S20 31 S19 OR S4

? rd

S21 26 RD (unique items)

? e lefta

Ref	Items	Index-term
E1	1	LEFT, POSITIVE-PRESSURE RESPIRATION
E2	1	LEFT, VENTRICULAR PRESSURE
E3	6	*LEFTA
E4	1	LEFTAESCENDING
E5	2	LEFTAFF
E6	1	LEFTAK
E7	8	LEFTAND
E8	2	LEFTANGLE
E9	1	LEFTANTERIOR
E10	2	LEFTANTERIORETEMPORAL
E11	1	LEFTANTERO
E12	1	LEFTARD

Enter P or PAGE for more

? s e3

S22 6 'LEFTA'

? e leftya

Ref	Items	Index-term
E1	1	LEFTY-2 ISOLATION
E2	1	LEFTY-2 PROTEIN
E3	36	*LEFTYA
E4	1	LEFTYA GENE
E5	1	LEFTYA PROTEIN
E6	2	LEFTYB
E7	1	LEFTYB PROTEIN
E8	1	LEFTYGENE
E9	9	LEFTYL



```

E10      1  LEFTYRAY
E11      2  LEFTYS
E12     229  LEFTY1

```

Enter P or PAGE for more

? s e3-e4

```

          36  LEFTYA
          1  LEFTYA GENE
S23      36  E3-E4

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? ds

Set	Items	Description
S1	21	'TGFB4'
S2	263	'TRANSFORMING GROWTH FACTOR BETA ANTIBODY'
S3	246	S2/1997:2006
S4	17	S2 NOT S3
S5	17	RD (unique items)
S6	125	E1-E8
S7	15	'TRANSFORMING GROWTH FACTOR BETA CDNA' OR E20-E26
S8	6	E13-E16
S9	3	'TRANSFORMING GROWTH FACTOR BETA NEUTRALIZING A'
S10	36	E2-E6
S11	3	'TRANSFORMING GROWTH FACTOR BETA 1 ANTIBODY'
S12	5	E34-E36
S13	1	'TRANSFORMING GROWTH FACTOR BETA 4 GENE'
S14	2	E39-E40
S15	18	'TRANSFORMING GROWTH FACTOR BETA4'
S16	1	'TRANSFORMING GROWTH FACTOR B4'
S17	215	S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16
S18	201	S17/1997:2006
S19	14	S17 NOT S18
S20	31	S19 OR S4
S21	26	RD (unique items)
S22	6	'LEFTA'
S23	36	E3-E4

? s s22 or s23

```

          6  S22
          36  S23
S24      42  S22 OR S23

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? s s24/1997:2006

Processing

Processed 10 of 25 files ...

>>>One or more prefixes are unsupported

>>> or undefined in one or more files.

>>>Year ranges not supported in one or more files

Completed processing all files

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          42  S24
          49018771  PY=1997 : PY=2006
S25      42  S24/1997:2006

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? ds

Set	Items	Description
S1	21	'TGFB4'
S2	263	'TRANSFORMING GROWTH FACTOR BETA ANTIBODY'
S3	246	S2/1997:2006
S4	17	S2 NOT S3
S5	17	RD (unique items)
S6	125	E1-E8
S7	15	'TRANSFORMING GROWTH FACTOR BETA CDNA' OR E20-E26
S8	6	E13-E16

S9 3 'TRANSFORMING GROWTH FACTOR BETA NEUTRALIZING A'  
 S10 36 E2-E6  
 S11 3 'TRANSFORMING GROWTH FACTOR BETA 1 ANTIBODY'  
 S12 5 E34-E36  
 S13 1 'TRANSFORMING GROWTH FACTOR BETA 4 GENE'  
 S14 2 E39-E40  
 S15 18 'TRANSFORMING GROWTH FACTOR BETA4'  
 S16 1 'TRANSFORMING GROWTH FACTOR B4'  
 S17 215 S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR  
       S15 OR S16  
 S18 201 S17/1997:2006  
 S19 14 S17 NOT S18  
 S20 31 S19 OR S4  
 S21 26 RD (unique items)  
 S22 6 'LEFTA'  
 S23 36 E3-E4  
 S24 42 S22 OR S23  
 S25 42 S24/1997:2006  
 ? t s21/3,kwic/all  
 >>>KWIC option is not available in file(s): 399

**21/3,KWIC/1 (Item 1 from file: 5)**

DIALOG(R)File 5:Biosis Previews(R)  
 (c) 2006 The Thomson Corporation. All rts. reserv.

0009999953 BIOSIS NO.: 199598467786

**Cloning and characterization of a human type II receptor for bone morphogenetic proteins**

AUTHOR: Rosenzweig Bradley L; Imamura Takeshi; Okadome Toshihide; Cox George N; Yamashita Hidetoshi; Ten Dijke Peter; Heldin Carl-Henrik; Miyazono Kohei (Reprint)  
 AUTHOR ADDRESS: Ludwig Inst. Cancer Res., Box 595, Biomedical Cent., S-751 24 Uppsala, Sweden\*\*Sweden  
 JOURNAL: Proceedings of the National Academy of Sciences of the United States of America 92 (17): p7632-7636 1995 1995  
 ISSN: 0027-8424  
 DOCUMENT TYPE: Article  
 RECORD TYPE: Abstract  
 LANGUAGE: English

DESCRIPTORS:

MISCELLANEOUS TERMS: ... TRANSFORMING GROWTH FACTOR BETA SUPERFAMILY

**21/3,KWIC/2 (Item 2 from file: 5)**

DIALOG(R)File 5:Biosis Previews(R)  
 (c) 2006 The Thomson Corporation. All rts. reserv.

0009815437 BIOSIS NO.: 199598283270

**Expression and localization of activin receptors in a human myeloid leukemia cell line, THP-1**

AUTHOR: Ying Shao-Yao; Zhang Zhong  
 AUTHOR ADDRESS: Dep. Cell Neurobiol., Univ. Southern California Med. Sch., 1333 San Pablo Street, BMT-401, Los Angeles, CA 90033, USA\*\*USA  
 JOURNAL: International Journal of Oncology 6 (4): p867-870 1995 1995  
 ISSN: 1019-6439  
 DOCUMENT TYPE: Article  
 RECORD TYPE: Abstract  
 LANGUAGE: English

DESCRIPTORS:

MISCELLANEOUS TERMS: ... **TRANSFORMING GROWTH FACTOR BETA SUPERFAMILY**

**21/3,KWIC/3 (Item 3 from file: 5)**

DIALOG(R)File 5:Biosis Previews(R)

(c) 2006 The Thomson Corporation. All rts. reserv.

0009687859 BIOSIS NO.: 199598155692

**Minisatellite loci as genetic markers in the chicken genome**

AUTHOR: Hanotte O; Gibbs M; Thomson P; Dawson D; McCamley C; Pugh A; Burke T

AUTHOR ADDRESS: Univ. Leicester, Dep. Zool., University Rd., Leicester, UK  
\*\*UK

JOURNAL: Animal Genetics 25 (SUPPL. 2): p48 1994 1994

CONFERENCE/MEETING: 24th Conference of the International Society for Animal Genetics Prague, Czech Republic July 23-29, 1994; 19940723

ISSN: 0268-9146

DOCUMENT TYPE: Meeting; Meeting Abstract

RECORD TYPE: Citation

LANGUAGE: English

DESCRIPTORS:

MISCELLANEOUS TERMS: ... **TRANSFORMING GROWTH FACTOR BETA 4 GENE**

**21/3,KWIC/4 (Item 4 from file: 5)**

DIALOG(R)File 5:Biosis Previews(R)

(c) 2006 The Thomson Corporation. All rts. reserv.

0009337262 BIOSIS NO.: 199497358547

**Expression and growth inhibitory effect of decapentaplegic Vg-related protein 6: Evidence for a regulatory role in keratinocyte differentiation**

AUTHOR: Drozdoff Vladimir; Wall Nancy A; Pledger W J

AUTHOR ADDRESS: Dep. Cell Biol., Vanderbilt Univ. Sch. Med., Nashville, TN  
37232, USA\*\*USA

JOURNAL: Proceedings of the National Academy of Sciences of the United States of America 91 (12): p5528-5532 1994 1994

ISSN: 0027-8424

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

DESCRIPTORS:

MISCELLANEOUS TERMS: ... **TRANSFORMING GROWTH FACTOR BETA SUPER FAMILY**

**21/3,KWIC/5 (Item 5 from file: 5)**

DIALOG(R)File 5:Biosis Previews(R)

(c) 2006 The Thomson Corporation. All rts. reserv.

0008771429 BIOSIS NO.: 199395073695

**The gene for bone morphogenetic protein 2A (BMP2A) is localized to human chromosome 20p12 by radioactive and nonradioactive in situ hybridization**

AUTHOR: Rao V V N Gopal; Loeffler Christiane; Wozney John M; Hansmann Ingo (Reprint)

AUTHOR ADDRESS: Inst. Humangenetik Univ., Gosslerstrasse 12d, W-3400  
Goettingen, Germany\*\*Germany

JOURNAL: Human Genetics 90 (3): p299-302 1992

ISSN: 0340-6717

DOCUMENT TYPE: Article

RECORD TYPE: Abstract  
LANGUAGE: English

DESCRIPTORS:

MISCELLANEOUS TERMS: ... TRANSFORMING GROWTH FACTOR BETA SUPERFAMILY

21/3,KWIC/6 (Item 6 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)  
(c) 2006 The Thomson Corporation. All rts. reserv.

0008195629 BIOSIS NO.: 199293038520

**KUPFFER CELLS FROM CARBON TETRACHLORIDE-INJURED RAT LIVERS PRODUCE  
CHEMOTACTIC FACTORS FOR FIBROBLASTS AND MONOCYTES THE ROLE OF TUMOR  
NECROSIS FACTOR-ALPHA**

AUTHOR: ARMENDARIZ-BORUNDA J (Reprint); SEYER J M; POSTLETHWAITE A E; KANG  
A H

AUTHOR ADDRESS: VETERANS AFF MED CENT, RES SERV, 1030 JEFFERSON AVE,  
MEMPHIS, TENN 38104, USA\*\*USA

JOURNAL: Hepatology 14 (5): p895-900 1991

ISSN: 0270-9139

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: ENGLISH

DESCRIPTORS: TRANSFORMING GROWTH FACTOR BETA MONONUCLEAR MACROPHAGIC CELL

21/3,KWIC/7 (Item 7 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)  
(c) 2006 The Thomson Corporation. All rts. reserv.

0007632024 BIOSIS NO.: 199191014915

**PRODUCTION OF INSULIN-LIKE GROWTH FACTOR BINDING PROTEINS IGFBPS BY PORCINE  
GRANULOSA CELLS IDENTIFICATION OF IGFBP-2 AND 3 AND REGULATION BY  
HORMONES AND GROWTH FACTORS**

AUTHOR: MONDSCHNEIN J S (Reprint); SMITH S A; HAMMOND J M

AUTHOR ADDRESS: HERSHEY MEDICAL CENTER, PENNSYLVANIA STATE UNIVERSITY, PO  
BOX 850, HERSHEY, PA 17033, USA\*\*USA

JOURNAL: Endocrinology 127 (5): p2298-2306 1990

ISSN: 0013-7227

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: ENGLISH

DESCRIPTORS: TRANSFORMING GROWTH FACTOR BETA FSH IMMUNOREACTIVITY

21/3,KWIC/8 (Item 1 from file: 34)

DIALOG(R)File 34:SciSearch(R) Cited Ref Sci  
(c) 2006 Inst for Sci Info. All rts. reserv.

05353035 Genuine Article#: VT054 No. References: 61

**Title: GLIAL-CELL LINE-DERIVED NEUROTROPHIC FACTOR PROMOTES THE DEVELOPMENT  
OF ADRENERGIC-NEURONS IN MOUSE NEURAL CREST CULTURES**

Author(s): MAXWELL GD; REID K; ELEFANTY A; BARTLETT PF; MURPHY M

Corporate Source: UNIV CONNECTICUT,CTR HLTH,DEPT ANAT,263 FARMINGTON  
AVE/FARMINGTON//CT/06032; ROYAL MELBOURNE HOSP,WALTER & ELIZA HALL INST  
MED RES/PARKVILLE/VIC 3052/AUSTRALIA/

Journal: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED

STATES OF AMERICA, 1996, V93, N23 (NOV 12), P13274-13279  
ISSN: 0027-8424  
Language: ENGLISH Document Type: ARTICLE (Abstract Available)

21/3,KWIC/9 (Item 2 from file: 34)  
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci  
(c) 2006 Inst for Sci Info. All rts. reserv.

03350577 Genuine Article#: NY669 No. References: 27  
**Title: EXPRESSION OF BONE MORPHOGENETIC PROTEIN GENES IN THE HUMAN DENTAL-PULP CELLS**  
Author(s): TAKEDA K; OIDA S; GOSEKI M; IIMURA T; MARUOKA Y; AMAGASA T; SASAKI S  
Corporate Source: TOKYO MED & DENT UNIV,FAC DENT,DEPT BIOCHEM,BUNKYO KU,1-5-45 YUSHIMA/TOKYO 113//JAPAN/; TOKYO MED & DENT UNIV,FAC DENT,DEPT BIOCHEM,BUNKYO KU/TOKYO 113//JAPAN/; TOKYO MED & DENT UNIV,FAC DENT,DEPT ORAL & MAXILLOFACIAL SURG 2/TOKYO 113//JAPAN/; TOKYO MED & DENT UNIV,FAC DENT,DEPT ORAL & MAXILLOFACIAL SURG 1/TOKYO 113//JAPAN/  
Journal: BONE, 1994, V15, N5 (SEP-OCT), P467-470  
ISSN: 8756-3282  
Language: ENGLISH Document Type: NOTE (Abstract Available)

21/3,KWIC/10 (Item 1 from file: 73)  
DIALOG(R)File 73:EMBASE  
(c) 2006 Elsevier Science B.V. All rts. reserv.

06761297 EMBASE No: 1997042786  
**Transforming growth factor beta in diabetic nephropathy**  
Border W.A.; Yamamoto T.; Noble N.A.  
W.A. Border, Division of Nephrology, Univ. of Utah School of Medicine, 50 North Medical Drive, Salt Lake City, UT 84132 United States  
Diabetes/Metabolism Reviews ( DIABETES METAB. REV. ) (United Kingdom) 1996, 12/4 (309-339)  
CODEN: DMREE ISSN: 0742-4221  
DOCUMENT TYPE: Journal; Review  
LANGUAGE: ENGLISH  
NUMBER OF REFERENCES: 128

DRUG TERMS (UNCONTROLLED): transforming growth factor beta antagonist  
--pharmacology--pd; **transforming growth factor beta antibody**  
--pharmacology--pd

21/3,KWIC/11 (Item 2 from file: 73)  
DIALOG(R)File 73:EMBASE  
(c) 2006 Elsevier Science B.V. All rts. reserv.

06717049 EMBASE No: 1996190191  
**Marked diversity in the action of growth factors on N-methyl-D-aspartate-induced neuronal degeneration**  
Prehn J.H.M.  
J.H.M. Prehn, Dept. of Pharmacology and Toxicology, Philipps-University, Ketzerbach 63, D-35052 Marburg Germany  
European Journal of Pharmacology ( EUR. J. PHARMACOL. ) (Netherlands) 1996, 306/1-3 (81-88)  
CODEN: EJPHA ISSN: 0014-2999  
DOCUMENT TYPE: Journal; Article

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

...DRUG TERMS (UNCONTROLLED): brain derived neurotrophic factor--drug toxicity--to; recombinant brain derived neurotrophic factor--drug comparison--cm; **transforming growth factor beta antibody** --pharmacology --pd; **transforming growth factor beta antibody** --drug interaction--it

21/3,KWIC/12 (Item 3 from file: 73)

DIALOG(R) File 73:EMBASE

(c) 2006 Elsevier Science B.V. All rts. reserv.

06421169 EMBASE No: 1996077869

**Transforming growth factor-beta in in vivo resistance**

Teicher B.A.; Holden S.A.; Ara G.; Chen G.

Dana-Farber Cancer Institute, Joint Center for Radiation Therapy, 44

Binney Street, Boston, MA 02115 United States

Cancer Chemotherapy and Pharmacology ( CANCER CHEMOTHER. PHARMACOL. ) ( Germany) 1996, 37/6 (601-609)

CODEN: CCPHD ISSN: 0344-5704

DOCUMENT TYPE: Journal; Article

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

DRUG TERMS (UNCONTROLLED): **transforming growth factor beta antibody** --drug toxicity--to; **transforming growth factor beta antibody** --pharmacology--pd; **transforming growth factor beta antibody** --drug therapy--dt; **transforming growth factor beta antibody** --drug dose--do

21/3,KWIC/13 (Item 4 from file: 73)

DIALOG(R) File 73:EMBASE

(c) 2006 Elsevier Science B.V. All rts. reserv.

06350226 EMBASE No: 1996003775

**Anti-(transforming growth factor beta) antibodies with predefined specificity inhibit metastasis of highly tumorigenic human xenotransplants in nu/nu mice**

Hoefer M.; Anderer F.A.

Friedrich-Miescher-Laboratorium, Max-Planck-Gesellschaft, Spemannstrasse 37/39, D-72076 Tübingen Germany

Cancer Immunology Immunotherapy ( CANCER IMMUNOL. IMMUNOTHER. ) (Germany) 1995, 41/5 (302-308)

CODEN: CIIMD ISSN: 0340-7004

DOCUMENT TYPE: Journal; Article

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

DRUG TERMS (UNCONTROLLED): **transforming growth factor beta antibody** --pharmacology--pd; **transforming growth factor beta antibody** --drug development--dv; **transforming growth factor beta antibody** --drug dose--do

21/3,KWIC/14 (Item 5 from file: 73)

DIALOG(R) File 73:EMBASE

(c) 2006 Elsevier Science B.V. All rts. reserv.

06155894 EMBASE No: 1995181304

**Perspectives in the treatment of liver fibrosis**

Mavrier P.; Mallat A.

Unite d'Hepatology, Hopital Henri-Mondor, 94010 Creteil France

Journal of Hepatology, Supplement ( J. HEPATOL. SUPPL. ) (Denmark) 1995

, 22/2 (111-1115)  
CODEN: JHSUF ISSN: 0169-5185  
DOCUMENT TYPE: Journal; Review  
LANGUAGE: ENGLISH

DRUG TERMS (UNCONTROLLED): s 0885--pharmacology--pd; s 0885--drug therapy  
--dt; **transforming growth factor beta antibody** --pharmacology--pd

21/3,KWIC/15 (Item 6 from file: 73)  
DIALOG(R)File 73:EMBASE  
(c) 2006 Elsevier Science B.V. All rts. reserv.

06046762 EMBASE No: 1995077061

**Expression of tissue-type plasminogen activator and its inhibitor couples with development of capillary network by human microvascular endothelial cells on matrigel**

Ito K.-I.; Ryuto M.; Ushiro S.; Ono M.; Sugeno A.; Kuraoka A.; Shirata Y.; Kuwano M.

Department of Biochemistry, Kyushu University, School of Medicine,  
Maidashi, Fukuoka 812 Japan  
Journal of Cellular Physiology ( J. CELL. PHYSIOL. ) (United States)  
1995, 162/2 (213-224)

CODEN: JCLLA ISSN: 0021-9541  
DOCUMENT TYPE: Journal; Article  
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

DRUG TERMS (UNCONTROLLED): tissue plasminogen activator inhibitor  
--endogenous compound--ec; **transforming growth factor beta antibody**

21/3,KWIC/16 (Item 7 from file: 73)  
DIALOG(R)File 73:EMBASE  
(c) 2006 Elsevier Science B.V. All rts. reserv.

05890565 EMBASE No: 1994297269

**Characterization of the influence of anti-hormone and/or anti-growth factor neutralizing antibodies on cell clone architecture and the growth of human neoplastic astrocytic cell lines**

Camby I.; Salmon I.; Rorive S.; Gras T.; Darro F.; Kruczynski A.; Danguy A.; Pasteels J.-L.; Kiss R.

Laboratory of Histology, Faculty of Medicine, Free University of  
Brussels, 808 Route de Lennik, 1070 Brussels Belgium  
Journal of Neuro-Oncology ( J. NEURO-ONCOL. ) (United States) 1994, 20/1  
(67-80)

CODEN: JNODD ISSN: 0167-594X  
DOCUMENT TYPE: Journal; Article  
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

DRUG TERMS (UNCONTROLLED): epidermal growth factor antibody; gastrin  
antibody; transforming growth factor alpha antibody; **transforming growth factor beta antibody**

21/3,KWIC/17 (Item 8 from file: 73)  
DIALOG(R)File 73:EMBASE  
(c) 2006 Elsevier Science B.V. All rts. reserv.

05796586 EMBASE No: 1994184909

**Immunosuppressive effects of 1.25-dihydroxyvitamin D<sub>3</sub> and its**

**analogue calcipotriol on epidermal cells**

Bagot M.; Charue D.; Leschs M.-C.; Pamphile R.; Revuz J.  
Department of Dermatology, Henri Mondor Hospital, 51 Av. Marechal de  
Lattre Tassigny, 94010 Creteil France  
British Journal of Dermatology ( BR. J. DERMATOL. ) (United Kingdom)  
1994, 130/4 (424-431)  
CODEN: BJDEA ISSN: 0007-0963  
DOCUMENT TYPE: Journal; Article  
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

DRUG TERMS (UNCONTROLLED): **transforming growth factor beta antibody**  
--pharmacology--pd; **transforming growth factor beta antibody** --drug  
interaction--it; **transforming growth factor beta antibody** --drug  
combination--cb

**21/3,KWIC/18 (Item 9 from file: 73)**

DIALOG(R)File 73:EMBASE

(c) 2006 Elsevier Science B.V. All rts. reserv.

05638040 EMBASE No: 1994044273

**Transforming growth factor-beta activity is increased in peritoneal fluid  
from women with endometriosis**

Oosterlynck D.J.; Meuleman C.; Waer M.; Koninckx P.R.  
Department of Obstetrics/Gynecology, University Hospital Gasthuisberg, 49  
Herestraat, 3000 Leuven Belgium  
Obstetrics and Gynecology ( OBSTET. GYNECOL. ) (United States) 1994,  
83/2 (287-292)  
CODEN: OBGNA ISSN: 0029-7844  
DOCUMENT TYPE: Journal; Article  
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

DRUG TERMS (UNCONTROLLED): **transforming growth factor beta antibody**

**21/3,KWIC/19 (Item 10 from file: 73)**

DIALOG(R)File 73:EMBASE

(c) 2006 Elsevier Science B.V. All rts. reserv.

05551533 EMBASE No: 1993319633

**Effect of antibody to transforming growth factor beta on bleomycin  
induced accumulation of lung collagen in mice**

Giri S.N.; Hyde D.M.; Hollinger M.A.  
Dept. Vet. Pharmacology/Toxicology, School of Veterinary Medicine,  
University of California, Davis, CA 95616 United States  
Thorax ( THORAX ) (United Kingdom) 1993, 48/10 (959-966)  
CODEN: THORA ISSN: 0040-6376  
DOCUMENT TYPE: Journal; Article  
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

DRUG TERMS (UNCONTROLLED): **transforming growth factor beta antibody** --drug  
therapy--dt

**21/3,KWIC/20 (Item 11 from file: 73)**

DIALOG(R)File 73:EMBASE

(c) 2006 Elsevier Science B.V. All rts. reserv.

05551530 EMBASE No: 1993319630



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<u>#3</u> Related Articles for PubMed (Select 9665343)		14:10:55	<u>29</u>

□ 1: Ann N Y Acad Sci. 1990;593:1-6.

Related Articles, Links

**The transforming growth factor-betas: past, present, and future.**

**Sporn MB, Roberts AB.**

Laboratory of Chemoprevention, National Cancer Institute, Bethesda, Maryland 20892.

Publication Types:

- Historical Article
- Review

[First Hit](#)[Previous Doc](#)[Next Doc](#)[Go to Doc#](#)

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L2: Entry 2 of 155

File: PGPB

May 11, 2006

DOCUMENT-IDENTIFIER: US 20060099576 A1

TITLE: Method for diagnosing a pre-neoplastic or neoplastic lesion in transitional epithelial cells

Brief Summary Text:

[0014] Recently, a new member of the TGF-.beta. superfamily, lefty-1, was recognized for its distinct asymmetric expression in gastrulating mouse embryos (Meno et al., 1996). Lefty-A is the human homologue of lefty-1. Lefty-A is also known as endometrial bleeding associated factor (ebaf) protein, which is associated with abnormal endometrial bleeding (Kothapalli et al., 1997). Ebaf is highly expressed in human endometrium prior to and during menstrual bleeding or abnormal uterine bleeding (Kothapalli et al., 1997). The amino acid sequence of the ebaf protein shows homology with, and structural features of, members of the TGF-.beta. superfamily (Kothapalli et al., 1997), and ebaf is also recognized as a member of the TGF-.beta. superfamily.

Brief Summary Text:

[0015] The ebaf gene is located on human chromosome 1, at band q42.1, and its nucleotide and deduced amino acid sequences are known. In view of the similarity in the nucleotide sequences of lefty-1 and ebaf, Kosaki et al. (1999) hypothesized that there may be mutations in the ebaf sequence in patients with laterality defects. Kosaki et al. (1999) went on to show that mutations in the ebaf gene are associated with left-right axis malformations in humans. A second human gene, lefty-B, also has been described. In mice, both the lefty-1 gene and the lefty-2 gene reside on chromosome 1H2. In humans, both the lefty-A (ebaf) gene and the lefty-B gene map to human syntenic region 1q42, and are separated from each other by 50 kb. The nucleotide sequences of lefty-A (ebaf) and lefty-B are 97% identical, so these proteins are more closely related to each other than to either of the mouse homologues.

Brief Summary Text:

[0016] It is known that ebaf mRNA is highly expressed in neoplastic cells that give rise to adenocarcinomas originating from the colon, ovary, pancreas, and testis (Tabibzadeh et al., 1997; U.S. Pat. No. 5,916,751). It is also known that other members of the TGF-.beta. superfamily have been found in human bladder carcinomas (Miyamoto et al., 1995; and Eder et al., 1996). However, prior to the present invention, it was not known that ebaf protein is highly expressed in cells of transitional-cell carcinomas and atypia/dysplasia of transitional epithelium. Moreover, prior to the present invention, it was not known that ebaf is secreted into bodily fluids, particularly the urine.

Brief Summary Text:

[0017] The present invention is based upon the discovery that endometrial bleeding associated factor (ebaf), a secreted protein, is found in the urine of subjects who have transitional-cell carcinoma (TCC) of the bladder. This discovery has broad implications in the diagnosis and treatment of TCCs of the urinary tract, and in the monitoring of TCC therapy.

Brief Summary Text:

[0018] Accordingly, it is an object of the present invention to provide a method

for determining whether a subject has a pre-neoplastic or neoplastic lesion in transitional epithelial cells, by assaying a diagnostic sample of the subject for ebaf expression, wherein ebaf expression elevated above normal is diagnostic of a pre-neoplastic or neoplastic lesion in transitional epithelial cells.

Brief Summary Text:

[0019] It is also an object of the present invention to provide a method for assessing the efficacy of therapy to treat a pre-neoplastic or neoplastic lesion in transitional epithelial cells in a subject who has undergone or is undergoing treatment for a pre-neoplastic or neoplastic lesion in transitional epithelial cells, by assaying a diagnostic sample of the subject for ebaf expression, wherein normal ebaf expression is indicative of successful therapy to treat a pre-neoplastic or neoplastic lesion in transitional epithelial cells, and ebaf expression elevated above normal is indicative of a need to continue therapy to treat a pre-neoplastic or neoplastic lesion in transitional epithelial cells.

Brief Summary Text:

[0020] Finally, it is an object of the present invention to provide a method for assessing the prognosis of a subject who has a pre-neoplastic or neoplastic lesion in transitional epithelial cells, by assaying a diagnostic sample of the subject for ebaf expression, wherein the subject's prognosis improves with a decrease in ebaf expression in the diagnostic sample of the subject.

Description of Disclosure:

[0022] FIG. 1 shows that ebaf proteins are secreted. Lanes 1 and 2: .sup.35S methionine-labeled ebaf was immunoprecipitated from the culture medium of human embryonic kidney epithelial (HEK)-293 cells (lane 1) or HEK-293 cells transfected with ebaf (lane 2) using A351 anti-ebaf antibody--the rabbit polyclonal antibody to the carboxy-terminus (C-terminus) of ebaf (amino acid residues 351-367). The immunoprecipitates then were subjected to SDS-PAGE, followed by autoradiography. Lanes 3 and 4: Ebaf in the culture medium of HEK-293 cells (lane 3) or HEK-293 cells transfected with ebaf (lane 4) was immunoaffinity-purified and subjected to SDS-PAGE, followed by Western blotting using the A351 antibody. Numbers at the left of the figure correspond with the molecular weights (in kD) of ebaf in its precursor and processed forms. IP: immunoprecipitate; WB: Western blotting

Description of Disclosure:

[0023] FIG. 2 depicts detection of ebaf protein by the A351 and A31 antibodies. A31 is the rabbit polyclonal antibody to the amino-terminus (N-terminus) of ebaf (amino acid residues 31-43). Ebaf protein was affinity-purified from the culture media of HEK-293 cells transfected using the A351 (lanes 1 and 3) or the A31 (lanes 2 and 4) antibody. 200 ng of the purified protein were subjected to Western blotting. The blots were probed with A351 (lanes 1 and 2) or A31 (lanes 3 and 4) antibodies. Numbers at the left of the figure correspond with the molecular weights (in kD) of ebaf in its precursor and processed forms.

Description of Disclosure:

[0024] FIG. 3 illustrates the identification of the endoproteolytic cleavage sites of ebaf. Ebaf shows two potential convertase cleavage sites: RGKR (amino acid residues 74-77) and RHGR (amino acid residues 132-135). HEK-293 cells were transfected with wild-type or mutated GGKG (amino acid residues 74-77) and GHGR (amino acid residues 132-135) forms of ebaf. The effect of these mutations on ebaf processing was analyzed by Western blotting using anti-ebaf antibody, A351. Numbers at the left of the figure correspond with the molecular weights (in kD) of ebaf in its precursor and processed forms.

Description of Disclosure:

[0025] FIG. 4 illustrates that ebaf is a glycosylated protein. A: The conditioned medium of HEK-293 cells stably transfected with ebaf sense cDNA (lanes 1 and 3) and HEK-293 cells transiently transfected with ebaf sense cDNA from several clones

mutated at the potential glycosylation site (lanes 2 and 4) were subjected to Western blotting. The blot was stained with the A351 polyclonal antibody. Molecular weights are shown in kD. B: The conditioned medium of HEK-293 cells stably transfected with ebaf sense cDNA was incubated without (lane 1) and with Endo H (lane 2) and with PNGase (lane 3), as described in the text, and then was subjected to Western blotting. The blot was stained with the A351 antibody. Molecular weights are shown in kD.

Description of Disclosure:

[0026] FIG. 5 shows the presence of ebaf protein in bladder carcinomas. 20 .mu.g of tissue lysate from a normal bladder mucosa (lane 1) and bladder carcinomas (lanes 2-8) were subjected to Western blotting. The blot was probed with A351 anti-ebaf antibody. Numbers at the left of the figure correspond with the molecular weights (in kD) of ebaf in its precursor and processed forms.

Description of Disclosure:

[0027] FIG. 6 also shows the presence of ebaf protein in bladder carcinomas. A: 20 ng of purified ebaf (lane 1), and 20 .mu.g of protein from tissue lysates from bladder carcinomas (lanes 2, 4, and 6) and from adjacent normal bladder mucosa (lanes 3, 5, and 7), were subjected to Western blotting. The blots were probed with A351 anti-ebaf antibody. Molecular weights are shown in kD. B: Sections of a urothelial mucosa lined with atypical epithelium (panels A and C) or adjacent papillary transitional-cell carcinoma (panels B and D) were immunostained for ebaf using A351 antibody. Arrows point to some of the strongly stained cells. The dotted lines in panels A and C show the boundaries of the surface epithelium. The dashed lines in panels B and D show the boundaries of the papillary carcinomas. SE: surface epithelium; LP: lamina propria; C: core of a papillary structure

Description of Disclosure:

[0028] FIG. 7 shows ebaf present in urine of either normal subjects or patients with hyperplasia, atypia, and carcinoma of transitional epithelium. All molecular weights are in kD. FIG. 7A shows the presence of ebaf in the urine of normal subjects. Purified ebaf (lane 1), and ebaf purified from 2.5 ml of urine samples of normal subjects (lanes 2-25), were subjected to Western blotting. The blots were probed with A351 antibody. FIG. 7B shows the presence of ebaf in the urine of patients without and with atypia. Ebaf purified from 2.5 ml of urine samples taken from patients with chronic inflammation (lane 1), hyperplasia (lane 2), or atypia (lanes 4-7) was subjected to Western blotting. The blots were probed with A351 antibody. FIG. 7C shows the presence of ebaf in the urine of patients with transitional-cell carcinoma (TCC). Ebaf purified from 2.5 ml of urine samples taken from patients with low-grade papillary transitional-cell carcinomas (lanes 1-11), carcinoma in situ (lanes 12-13), or high-grade papillary transitional-cell carcinoma (lanes 14-17) was subjected to Western blotting. The blots were probed with A351 antibody. FIG. 7D shows the presence of ebaf in the urine of normal subjects and bladder cancer patients. Ebaf purified from urine (lanes 1-3) and concentrated urine (lanes 4-6) was subjected to Western blotting. The blots were probed with A351 antibody. Lanes 1 and 6 show ebaf in the urine from a normal subject. Lanes 2, 3, 4, 5 show ebaf in the urine from patients with papillary TCC.

Description of Disclosure:

[0029] FIG. 8 depicts ebaf protein in the sera of normal subjects and in the sera of patients with bladder carcinomas. All molecular weights are in kD. A: Purified ebaf (lane 1) and ebaf affinity-purified from sera of normal patients (lanes 2-3: male; lane 4: female, day 3 of the menstrual cycle; lane 5: female, day 3 after ovulation; lane 6: female, day 10 after ovulation; lane 7: female, first day of menses) and bladder cancer patients (lanes 8-14) were subjected to Western blotting. The blots were probed with A351 anti-ebaf antibody. B: Purified ebaf (lane 1) and ebaf affinity-purified from urine (upper panel) and sera (lower panel) of control patient without TCC (lane 2) and with TCC (lanes 3-9) were subjected to Western blotting. The blots were probed with A351 anti-ebaf antibody.

Description of Disclosure:

[0030] FIG. 9 depicts the nucleotide sequence and corresponding amino acid sequence for ebaf.

Description of Disclosure:

[0031] The present invention provides a method for determining whether a subject has a pre-neoplastic or neoplastic lesion in transitional epithelial cells. As used herein, the "subject" is a mammal, including, without limitation, a cow, dog, human, monkey, mouse, pig, or rat, but is preferably a human. The method of the present invention comprises assaying a diagnostic sample of the subject for expression of endometrial bleeding associated factor (ebaf), wherein ebaf expression elevated above normal is diagnostic of a pre-neoplastic or neoplastic lesion in transitional epithelial cells.

Description of Disclosure:

[0032] Unless otherwise indicated, "ebaf" includes both an ebaf (lefty-A) protein and an "ebaf analogue". As used herein, "ebaf protein" includes the 42-kD pro-protein (precursor) form of ebaf, as disclosed herein, as well as the 34- and 28-kD C-terminus polypeptides processed from the precursor by proteolytic cleavage and any other forms of the precursor produced by post-translational modification (e.g., glycosylation, etc.). Ebaf protein has the amino acid sequence set forth in FIG. 9, or a portion thereof corresponding to the 34- or 28-kD processed forms of the protein. An "ebaf analogue", as used herein, is a variant of the ebaf protein that has 60% or greater (preferably, 70% or greater) amino-acid-sequence homology with the ebaf protein, as well as a variant of the ebaf protein that has a homologous three-dimensional conformation. Additionally, the term "ebaf analogue", as defined herein, includes peptides related to ebaf, particularly lefty-B, lefty-1, lefty-2, and other proteins that have an amino acid sequence similar to that of ebaf. Preferably, the ebaf analogue is lefty-B. Ebaf and ebaf analogues may be produced synthetically or recombinantly, or may be isolated from native cells. Ebaf is preferably produced recombinantly, using conventional techniques and cDNA encoding ebaf (FIG. 9).

Description of Disclosure:

[0036] According to the method of the present invention, the diagnostic sample of a subject may be assayed in vitro or in vivo. In accordance with the present invention, where the assay is performed in vitro, a diagnostic sample from the subject may be removed using standard procedures. The diagnostic sample may be tissue, particularly any transitional epithelium (including urothelial mucosa from any organ of the urinary tract and a tumor in any transitional epithelium), which may be removed by standard biopsy. In one embodiment of the present invention, the tissue is obtained from the bladder, pelvis of the kidney, ureter, or urethra of the subject. In addition, the diagnostic sample may be a bodily fluid, including cerebrospinal fluid, pericardial fluid, peritoneal fluid, saliva, serum, and urine. Furthermore, the diagnostic sample may be a cytological preparation. Where the diagnostic sample is a cytological preparation, cells (including cancer cells) sloughed off from the lining of the bladder, for example, and subsequently voided in the urine, may be examined in an assay for expression of ebaf. Such a cytological preparation is commonly used in current methods for diagnosing bladder cancer based on cell morphology.

Description of Disclosure:

[0037] Protein may be isolated and purified from the diagnostic sample of the present invention using standard methods known in the art, including, without limitation, extraction from a tissue (e.g., with a detergent that solubilizes the protein) where necessary, followed by affinity purification on a column, chromatography (e.g., FTLC and HPLC), immunoprecipitation (with an antibody to ebaf, such as A351 antibody, as described herein), and precipitation (e.g., with isopropanol and a reagent such as Trizol). Isolation and purification of the

protein may be followed by electrophoresis (e.g., on a SDS-polyacrylamide gel). Nucleic acid may be isolated from a diagnostic sample using standard techniques known to one of skill in the art.

Description of Disclosure:

[0038] In accordance with the method of the present invention, a pre-neoplastic or neoplastic lesion in transitional epithelial cells in a subject may be diagnosed by assaying a diagnostic sample of the subject for expression of ebaf, wherein ebaf expression elevated above normal is diagnostic of a pre-neoplastic or neoplastic lesion in transitional epithelial cells. As used herein, "expression" means the transcription of the ebaf gene into at least one mRNA transcript, or the translation of at least one mRNA into an ebaf protein, as defined above (i.e., the 42-kD ebaf precursor and any processed forms of ebaf resulting from post-translational modification, including the 34- and 28-kD forms resulting from cleavage of the precursor, as well as other forms produced by glycosylation and other types of modification). Accordingly, a diagnostic sample may be assayed for ebaf expression by assaying for ebaf protein (as defined above), cDNA, or mRNA. The appropriate form of ebaf will be apparent based on the particular techniques discussed herein. Furthermore, as described above, it is contemplated that the diagnostic sample may be assayed for expression of any or all forms of ebaf protein (including precursor, endoproteolytically-processed forms, and other forms resulting from post-translational modification) in order to determine whether a subject or patient has a pre-neoplastic or neoplastic lesion in transitional epithelial cells.

Description of Disclosure:

[0039] As used herein, "ebaf expression elevated above normal" means expression of ebaf at a level that is significantly greater than the level expected for the same type of diagnostic sample taken from a nondiseased subject or patient (i.e., one who does not have a pre-neoplastic or neoplastic lesion in transitional epithelial cells) of the same gender and of similar age. As further used herein, "significantly greater" means that the difference between the level of ebaf expression that is elevated above normal, and the expected (normal) level of ebaf, is of statistical significance. Preferably, ebaf expression elevated above normal is expression of ebaf at a level that is at least 10% greater than the level of ebaf expression otherwise expected. Where ebaf expression is expected to be absent from a particular diagnostic sample taken from a particular subject or patient, the normal level of ebaf expression for that subject or patient is nil. Where a particular diagnostic sample taken from a particular subject or patient is expected to have a low level of constitutive ebaf expression, that low level is the normal level of ebaf expression for that subject or patient. As disclosed herein, ebaf expression is generally absent, or present at very low levels, in the bladder tissue, serum, and urine of nondiseased control subjects.

Description of Disclosure:

[0040] Expected or normal levels of ebaf expression for a particular diagnostic sample taken from a subject or patient may be easily determined by assaying nondiseased subjects of a similar age and of the same gender. For example, diagnostic samples may be obtained from at least 30 normal, healthy men between the ages of 25 and 80, to determine the normal quantity of ebaf expression in males. However, to determine the normal quantity of ebaf expression in women, there is a need to collect samples at various stages of the female menstrual cycle, since ebaf is expressed during the late secretory and menstrual phases. Accordingly, diagnostic samples could be collected, for example, from a minimum of five women in each phase of the menstrual cycle--early proliferative, mid-proliferative, late proliferative, early secretory, mid-secretory, late secretory, and menstrual phases--for a total of 35 subjects.

Description of Disclosure:

[0041] Once the above-described samples have been obtained, the normal quantities

of ebaf expression in men and women may be determined using a standard assay for quantification, such as flow cytometry, Western blot analysis, or an ELISA for measuring protein quantities, as described below. For example, an ELISA may be run on each sample in duplicate, and the means and standard deviations of the quantity of the ebaf protein may be determined. If necessary, additional subjects may be recruited before the normal quantities of ebaf expression are quantified.

Description of Disclosure:

[0042] In accordance with the method of the present invention, a diagnostic sample of a subject may be assayed for ebaf expression using detection methods and assays readily determined from the known art, including, without limitation, immunological techniques, hybridization analysis, fluorescence imaging techniques, and/or radiation detection. For example, according to the method of the present invention, a diagnostic sample of the subject may be assayed for ebaf expression using an agent reactive with ebaf. As used herein, "reactive" means the agent has affinity for, binds to, or is directed against ebaf. As further used herein, an "agent" shall include a protein, polypeptide, peptide, nucleic acid (including DNA or RNA), antibody, Fab fragment, F(ab').sub.2 fragment, molecule, compound, antibiotic, drug, and any combinations thereof. A Fab fragment is a univalent antigen-binding fragment of an antibody, which is produced by papain digestion. A F(ab').sub.2 fragment is a divalent antigen-binding fragment of an antibody, which is produced by pepsin digestion. Preferably, the agent of the present invention is labeled with a detectable marker. The detection of ebaf expression in the method of the present invention then may be followed by an assay to measure or quantify the extent of ebaf expression in a diagnostic sample of a subject. Such assays are well known to one of skill in the art, and may include flow cytometry, mass spectroscopy, Western blot analysis, or an ELISA for measuring amounts of ebaf protein.

Description of Disclosure:

[0043] In one embodiment of the present invention, the agent reactive with ebaf is an antibody. As used herein, the antibody of the present invention may be polyclonal or monoclonal, and may be raised against any or all forms of ebaf protein (e.g., the 42-, 34-, or 28-kD protein). In addition, the antibody of the present invention may be produced by techniques well known to those skilled in the art. Polyclonal antibody, for example, may be produced by immunizing a mouse, rabbit, or rat with purified ebaf. Monoclonal antibody then may be produced by removing the spleen from the immunized mouse, and fusing the spleen cells with myeloma cells to form a hybridoma which, when grown in culture, will produce a monoclonal antibody. As disclosed herein, polyclonal anti-ebaf antibodies, A351 and A31, have been produced by immunizing a rabbit.

Description of Disclosure:

[0045] Where the agent of the present invention is an antibody reactive with ebaf, a diagnostic sample (e.g., urine) taken from the subject may be purified by passage through an affinity column which contains ebaf antibody as a ligand attached to a solid support, such as an insoluble organic polymer in the form of a bead, gel, or plate. The antibody attached to the solid support is used in the form of a column. Examples of suitable solid supports include, without limitation, agarose, cellulose, dextran, polyacrylamide, polystyrene, sepharose, or other insoluble organic polymers. The ebaf antibody may be further attached to the solid support through a spacer molecule, if desired. Appropriate binding conditions (e.g., temperature, pH, and salt concentration) may be readily determined by the skilled artisan. In a preferred embodiment, the ebaf antibody is attached to a sepharose column, such as Sepharose 4B. Alternatively, the diagnostic sample of the present invention may be concentrated in a concentration device, such as a Centricon-30 (Amicon Co., Beverly, Mass.), or other similar device. The molecular weight cutoff of the device may be 10,000 kD, for example.

Description of Disclosure:

[0046] Where the agent is an antibody, a diagnostic sample of the subject may be



assayed for ebaf expression using binding studies that utilize one or more antibodies immunoreactive with ebaf, along with standard immunological detection techniques. For example, the ebaf protein eluted from the affinity column, or the retentant in the concentrating device, may be subjected to an ELISA assay, Western blot analysis, flow cytometry, or any other immunostaining method employing an antigen-antibody interaction. Preferably, the diagnostic sample is assayed for ebaf expression using Western blotting.

Description of Disclosure:

[0047] Alternatively, a diagnostic sample of a subject may be assayed for ebaf expression using hybridization analysis of nucleic acid extracted from the diagnostic sample taken from the subject. According to this method of the present invention, the hybridization analysis may be conducted using Northern blot analysis of mRNA. This method also may be conducted by performing a Southern blot analysis of DNA using one or more nucleic acid probes which hybridize to nucleic acid encoding ebaf. The nucleic acid probes may be prepared by a variety of techniques known to those skilled in the art, including, without limitation, the following: restriction enzyme digestion of ebaf nucleic acid; and automated synthesis of oligonucleotides having sequences which correspond to selected portions of the nucleotide sequence of the ebaf nucleic acid, using commercially-available oligonucleotide synthesizers, such as the Applied Biosystems Model 392 DNA/RNA synthesizer.

Description of Disclosure:

[0048] The nucleic acid probes used in the present invention may be DNA or RNA, and may vary in length from about 8 nucleotides to the entire length of the ebaf nucleic acid. The ebaf nucleic acid used in the probes may be derived from mammalian ebaf. The nucleotide sequences for both mouse lefty-1 and human lefty-A (ebaf) are known (Meno et al., 1996; and Kothapalli et al., 1997). Using these sequences as probes, the skilled artisan could readily clone corresponding ebaf cDNA from other species. In addition, the nucleic acid probes of the present invention may be labeled with one or more detectable markers. Labeling of the nucleic acid probes may be accomplished using one of a number of methods known in the art--e.g., nick translation, end labeling, fill-in end labeling, polynucleotide kinase exchange reaction, random priming, or SP6 polymerase (for riboprobe preparation)--along with one of a variety of labels--e.g., radioactive labels, such as <sup>35</sup>S, <sup>32</sup>P, or <sup>3</sup>H, or nonradioactive labels, such as biotin, fluorescein (FITC), acridine, cholesterol, or carboxy-X-rhodamine (ROX). Combinations of two or more nucleic acid probes (or primers), corresponding to different or overlapping regions of the ebaf nucleic acid, also may be used to assay a diagnostic sample for ebaf expression, using, for example, PCR or RT-PCR.

Description of Disclosure:

[0049] It is contemplated that the diagnostic sample in the present invention frequently will be assayed for ebaf expression not by the subject or patient, nor by his/her consulting physician, but by a laboratory technician or other clinician. Accordingly, the method of the present invention further comprises providing to a subject's or patient's consulting physician a report of the results obtained upon assaying a diagnostic sample of the subject or patient for ebaf expression.

Description of Disclosure:

[0050] It is also within the confines of the present invention to use detected levels of ebaf expression in an assayed diagnostic sample as a clinical or pathologic staging tool. For example, as disclosed herein, ebaf levels detected in most diagnostic samples taken from patients who had low-grade transitional-cell carcinoma (TCC) of the bladder were lower than those detected in most diagnostic samples taken from patients with high-grade lesions, such as flat carcinoma in situ and high-grade papillary TCC of the bladder. Accordingly, detected levels of ebaf expression in an assayed diagnostic sample may be used to determine the grade or stage of the various tumors and lesions found in transitional epithelium of the

bladder and other organs of the urinary tract. In addition, detected levels of ebaf expression in an assayed diagnostic sample may be used to determine whether any treatment method is appropriate for a particular subject or patient who has a pre-neoplastic or neoplastic lesion in transitional epithelial cells.

Description of Disclosure:

[0051] Furthermore, it is within the confines of the present invention that detected levels of expression of each of the various forms of ebaf (e.g., the 42-, 34-, or 28-kD protein) in an assayed diagnostic sample of a subject or patient may be used to diagnose the particular type of transitional-cell carcinoma in the subject or patient, based upon their relative abundances. As disclosed herein, ebaf precursor and its endoproteolytically-processed forms may be detected in bladder carcinomas to differing extents, depending upon the type of bladder cancer in question. Accordingly, a determination of the extent to which each form of ebaf is expressed in a diagnostic sample of a subject or patient may provide an indication of the type of TCC found in the subject or patient.

Description of Disclosure:

[0052] The present invention further provides a method for assessing the efficacy of therapy to treat a pre-neoplastic or neoplastic lesion in transitional epithelial cells in a subject or patient who has undergone or is undergoing treatment for a pre-neoplastic or neoplastic lesion in transitional epithelial cells. The method of the present invention comprises assaying a diagnostic sample of the subject or patient for ebaf expression, wherein normal ebaf expression is indicative of successful therapy to treat the pre-neoplastic or neoplastic lesion in transitional epithelial cells, and ebaf expression elevated above normal is indicative of a need to continue therapy to treat the pre-neoplastic or neoplastic lesion in transitional epithelial cells. The pre-neoplastic or neoplastic lesion may be any of those described above, including TCC. The TCC may be a transitional-cell carcinoma of the urinary tract, including TCC of the bladder, pelvis of the kidney, ureter, or urethra (e.g., carcinoma in situ, papillary TCC, etc.), or a TCC of other tissues or organs, outside of the urinary tract, that are lined with transitional epithelium (e.g., the transitional zone between the anal canal and the colonic mucosa). The diagnostic sample may be tissue, a bodily fluid, or a cytological preparation, as described above. The diagnostic sample may be assayed for expression of ebaf in vitro or in vivo. In addition, the diagnostic sample may be assayed for expression of ebaf using all of the various assays and methods of detection and quantification described above. This method of the present invention provides a means of monitoring the effectiveness of therapy to treat a pre-neoplastic or neoplastic lesion in transitional epithelial cells by permitting the periodic assessment of levels of ebaf expression in a diagnostic sample taken from a subject or patient.

Description of Disclosure:

[0053] According to the method of the present invention, a diagnostic sample of a subject or patient may be assayed, and levels of ebaf expression may be assessed, at any time following the initiation of therapy to treat a pre-neoplastic or neoplastic lesion in transitional epithelial cells. For example, levels of ebaf expression may be assessed while the subject or patient is still undergoing treatment for a pre-neoplastic or neoplastic lesion in transitional epithelial cells. Where levels of ebaf expression detected in an assayed diagnostic sample of the subject or patient continue to remain elevated above normal, a physician may choose to continue with the subject's or patient's treatment for the pre-neoplastic or neoplastic lesion in transitional epithelial cells. Where levels of ebaf expression in an assayed diagnostic sample of the subject or patient decrease through successive assessments, it may be an indication that the treatment for a pre-neoplastic or neoplastic lesion in transitional epithelial cells is working, and that treatment doses could be decreased or even ceased. Where levels of ebaf in an assayed diagnostic sample of the subject or patient do not rapidly decrease through successive assessments, it may be an indication that the treatment for a

pre-neoplastic or neoplastic lesion in transitional epithelial cells is not working, and that treatment doses could be increased. Where ebaf expression is no longer detected in an assayed diagnostic sample of a subject or patient at levels elevated above normal, a physician may conclude that the treatment for a pre-neoplastic or neoplastic lesion in transitional epithelial cells has been successful, and that such treatment may cease.

Description of Disclosure:

[0054] It is also within the confines of the present invention to assess levels of ebaf expression following completion of the subject's or patient's treatment for a pre-neoplastic or neoplastic lesion in transitional epithelial cells, in order to determine whether the pre-neoplastic or neoplastic lesion in transitional epithelial cells has recurred in the subject or patient. Accordingly, an assessment of levels of ebaf expression in an assayed diagnostic sample may provide a convenient way to conduct follow-ups of patients with a pre-neoplastic or neoplastic lesion in transitional epithelial cells. Furthermore, as described above, it is within the confines of the present invention to use assessed levels of ebaf expression in an assayed diagnostic sample as a clinical or pathologic staging tool, as a means of determining the extent of the pre-neoplastic or neoplastic lesion in transitional epithelial cells in the subject or patient, and as a means of ascertaining appropriate treatment options.

Description of Disclosure:

[0055] It is contemplated that the diagnostic sample of the present invention frequently will be assayed for ebaf expression not by the subject or patient, nor by his/her consulting physician, but by a laboratory technician or other clinician. Accordingly, this method of the present invention further comprises providing to a subject's or patient's consulting physician a report of the results obtained upon assaying a diagnostic sample of the subject or patient for ebaf expression.

Description of Disclosure:

[0056] A correlation exists, in general, between tumor burden and the survival of a patient who has cancer. The mortality from cancer can be significantly reduced if tumors are found and treated at an early stage. As described below, ebaf expression is detected at low levels in the urine of patients with hyperplasia of the bladder transitional epithelium. Significantly higher levels of ebaf expression, however, are found in the urine of patients with flat carcinoma in situ in the bladder. Moreover, in the majority of patients who had low-grade papillary transitional-cell carcinoma of the bladder, amounts of ebaf detected in the urine were lower than those found in the urine of patients with high-grade carcinomas. Accordingly, the overexpression of ebaf correlates with the degree of morphologic differentiation of transitional-cell carcinomas, with those having a poor prognosis showing the potential to secrete more ebaf into the urine.

Description of Disclosure:

[0057] In view of the foregoing, it is also contemplated in the present invention that assaying a diagnostic sample for ebaf expression may be a useful tool for providing information concerning the prognosis of a subject or patient who has a pre-neoplastic or neoplastic lesion in transitional epithelial cells. Accordingly, the present invention further provides a method for assessing the prognosis of a subject who has a pre-neoplastic or neoplastic lesion in transitional epithelial cells, comprising assaying a diagnostic sample of the subject for ebaf expression, wherein the subject's prognosis improves with a decrease in ebaf expression in the diagnostic sample of the subject.

Description of Disclosure:

[0058] In accordance with the method of the present invention, the pre-neoplastic or neoplastic lesion in transitional epithelial cells may be any of those described above, including TCC. The TCC may be a transitional-cell carcinoma of the urinary tract, including TCC of the bladder, pelvis of the kidney, ureter, or urethra

(e.g., carcinoma in situ, papillary TCC, etc.), or a TCC of other tissues or organs, outside of the urinary tract, that are lined with transitional epithelium (e.g., the transitional zone between the anal canal and the colonic mucosa). The diagnostic sample may be tissue, a bodily fluid, or a cytological preparation, as described above. The diagnostic sample may be assayed in vitro or in vivo. In addition, the diagnostic sample may be assayed using all of the various assays and detection and quantification methods described above. This method of the present invention provides a means of determining the prognosis of a subject or patient diagnosed with a pre-neoplastic or neoplastic lesion in transitional epithelial cells based upon the level of ebaf expression in an assayed diagnostic sample of the subject or patient.

Description of Disclosure:

[0059] According to the method of the present invention, a diagnostic sample of a subject or patient may be assayed, and levels of ebaf expression may be assessed, at any time following the diagnosis of a pre-neoplastic or neoplastic lesion in transitional epithelial cells in the subject or patient. For example, levels of ebaf expression in an assayed diagnostic sample may be assessed before the subject or patient undergoes treatment for a pre-neoplastic or neoplastic lesion in transitional epithelial cells, in order to determine the subject's or patient's initial prognosis. Additionally, levels of ebaf expression in an assayed diagnostic sample may be assessed while the subject or patient is undergoing treatment for a pre-neoplastic or neoplastic lesion in transitional epithelial cells, in order to determine whether the subject's or patient's prognosis has become more or less favorable.

Description of Disclosure:

[0060] Where levels of ebaf expression detected in an assayed diagnostic sample of the subject or patient continue to remain significantly elevated above normal, a physician may conclude that the subject's or patient's prognosis is poor. Where levels of ebaf expression in an assayed diagnostic sample of the subject or patient decrease through successive assessments, it may be an indication that the subject's or patient's prognosis is improving. Where levels of ebaf in an assayed diagnostic sample of the subject or patient do not decrease significantly through successive assessments, it may be an indication that the subject's or patient's prognosis is not improving. Where ebaf expression is no longer detected in an assayed diagnostic sample of the subject or patient at levels significantly elevated above normal, a physician may conclude that the subject's or patient's prognosis is favorable.

Description of Disclosure:

[0061] It is contemplated that the diagnostic sample of the present invention frequently will be assayed for ebaf expression not by the subject or patient, nor by his/her consulting physician, but by a laboratory technician or other clinician. Accordingly, the method of the present invention further comprises providing to a subject's or patient's consulting physician a report of the results obtained upon assaying a diagnostic sample of the subject or patient for ebaf expression.

Description of Disclosure:

[0062] The discovery that ebaf can be detected at above-normal levels in the bodily fluids and tissues of subjects suffering from TCC or pre-neoplastic lesions in transitional epithelial cells provides a means for identifying patients with TCC or pre-neoplastic lesions in transitional epithelial cells, and presents the potential for commercial application in the form of a noninvasive urine or serum test (or a test involving another bodily fluid) for the diagnosis of pre-neoplastic lesions in transitional epithelial cells, and TCC of the urinary tract and of other tissues and organs that are lined with transitional epithelium. The development of such a test could provide general mass-screening procedures. Such procedures may be used for mass screening of the general population, and for screening subjects or patients who have no symptoms or signs of disease. General mass-screening procedures can assist in the early detection and diagnosis of such cancers, and can

provide a method for the follow-up of patients in whom above-normal ebaf expression has been detected. Accordingly, the present invention further provides a kit for use as an assay of pre-neoplastic and neoplastic lesions in transitional epithelial cells, comprising an agent reactive with ebaf. The agent may be any of those described above, and may be used in any of the above-described assays or methods for detecting or quantifying ebaf expression. In addition, the kit may detect any or all forms of ebaf (e.g., the 42-, 34-, or 28-kD protein) or fragments thereof.

Description of Disclosure:

[0064] Ebaf (lefty-A) is a member of the family of morphogens that direct the left-right (L-R) asymmetry of the vertebrate body plan from an originally symmetric embryo (Meno et al., 1996, 1997, 1998; and Kothapalli et al., 1997). Consistent with a role in the development of laterality, Kosaki et al. (1999) reported that ebaf, the presumed human homologue of mouse lefty-1, carries mutations in individuals who show abnormal axis development. However, there are clear indications that this embryonic signal continues, during adulthood, to regulate multiple functions in a variety of organs.

Description of Disclosure:

[0065] Ebaf was originally cloned as a human homologue of lefty-1 for its role in normal and abnormal uterine bleeding. For this reason, it is also known as endometrial bleeding associated factor (ebaf). More recently, it was discovered that lefty-1 transcript and translation products are induced during the course of osteoblastic cell differentiation. Lefty-1 modulated the induction of alkaline phosphatase (ALP) by these cells (Seth et al., 2000). These findings show that the ebaf gene does not become silent after embryonic development, and is likely to continue to function throughout life. Besides these pleiotropic actions in homeostasis of normal tissues, ebaf is considered to play a part in the pathogenesis of a distinct group of tumors. Specifically, it is known that ebaf mRNA is highly expressed in the neoplastic cells that give rise to adenocarcinomas originating from colon, ovary, pancreas, and testis (Tabibzadeh et al., 1997; U.S. Pat. No. 5,916,751). In contrast, ebaf is not expressed in nonepithelial tumors, such as melanoma, sarcoma, and lymphoma. Prior to the present invention, there was no evidence that ebaf protein is synthesized, processed, and released by the cells of transitional-cell carcinomas or atypia/dysplasia of transitional epithelium. Moreover, prior to the present invention, there was no evidence that ebaf is secreted into bodily fluids, particularly the urine.

Description of Disclosure:

[0066] TGF- $\beta$ . superfamily members are all processed before activation, suggesting that protein cleavage is an essential step for ebaf activation and, consequently, for cell signaling. Like many other proteins, members of the TGF- $\beta$ . superfamily are synthesized as large, inactive precursor proteins, that must be proteolytically processed to release the bioactive polypeptides (Sha et al., 1989). Among the members of the TGF- $\beta$ . super-family, processing of the TGF- $\beta$ .1 precursor has been widely studied. Based on the findings, it is clear that proteolytic cleavage by a convertase, furin, is an essential step in the formation of the biologically-active TGF- $\beta$ .1 polypeptide.

Description of Disclosure:

[0067] TGF- $\beta$ .1 is expressed as an inactive 55-kD precursor protein that, after enzymatic cleavage, produces a 12.5-kD carboxy-terminus polypeptide that, once dimerized, forms a 25-kD biologically-active homodimer (Dubois et al., 1995). However, despite its biological importance, virtually nothing is known about the endoproteolytic cleavage of ebaf protein, and the biological activity of its released form. Accordingly, the inventor has analyzed herein the secretion and cleavage of ebaf, and have identified the cleavage sites of the ebaf protein. Because bladder cancer remains a common cancer in both women and men (Metts et al., 2000), the inventor used transitional-cell carcinoma (TCC) of the bladder as a paradigm to assess synthesis and release of ebaf. To determine that the cleavage of

ebaf in bladder carcinomas releases biologically-active products, the transforming ability of ebaf purified from urine of bladder cancer patients was compared to the activity of a recombinant ebaf protein.

Description of Disclosure:

[0068] The full length, 1.961-kb ebaf (lefty-A) cDNA was derived from a human placental cDNA library (Lamb et al., 1993). A 1.1-kb cDNA fragment of glyceraldehyde 3-phosphate dehydrogenase (GAPDH) was obtained from Clontech (Palo Alto, Calif.). Other materials included deoxycytidine 5'-triphosphate dCTP .alpha.-.sup.32P (3000 Ci/mmol) (Dupont NEN Research Products, Boston, Mass.), Prime-a-Gene labeling kit (Promega, Madison, Wis.), Nick column (Pharmacia Biotech, Piscataway, N.J.), Hybond nylon membrane and enhanced chemiluminescence system (Amersham, Arlington Heights, Ill.), Kodak-OMAT films (Sigma Chemical Company, St. Louis, Mo.), Coomassie Plus Protein Assay Reagent (Pierce, Rockford, Ill.), nitrocellulose membrane (MSI, Westborough, Mass.), biotin-labeled goat anti-rabbit antiserum and avidin-biotin complex (ABC) reagent (Vector Laboratories, Burlingame, Calif.), Protein G Plus Agarose (Santa Cruz Biotechnology, Santa Cruz, Calif.), enhanced chemiluminescence system (Boehringer Mannheim, Indianapolis, Ind.), PVDF membranes (Bio-Rad Laboratories, Hercules, Calif.), and Kodak-OMAT films (Sigma Chemical Company, St. Louis, Mo.). Chinese hamster ovary (CHO) and human embryonic kidney epithelial (HEK)-293 cells were obtained from American Type Culture Collection (Manassas, Va.). All other chemicals were obtained from either Sigma Chemical Company or Fisher Scientific (Pittsburgh, Pa.).

Description of Disclosure:

[0070] Cultured cells were maintained in DMEM medium (Life Technologies, Inc., Rockville, Md.) supplemented with 10% fetal bovine serum (Life Technologies, Inc., Rockville, Md.) and 1% antibiotic-antimycotic mixture (Life Technologies, Inc., Rockville, Md.). For transfection, CHO cells were seeded into 6-well plates (Falcon, Franklin Lakes, N.J.), at a concentration of 1.3.times.10.sup.4 cells/ml, and maintained in a CO.sub.2 chamber at 37.degree. C. for about 16 h. When 60% confluent, cells were transfected with cDNA of ebaf, using Superfect Transfect Reagent (Qiagen, Valencia, Calif.) or fugene (Boehringer Mannheim, Germany) following the manufacturer's protocol. The amount of proteins in the cell, cytosolic lysates, or nuclear lysates was determined by the Bio-Rad Protein Assay kit (Bio-Rad Laboratories, Hercules, Calif.).

Description of Disclosure:

[0072] The ebaf (lefty-A) cDNA was originally cloned in a pBluescript.RTM. SK.sup.- vector. A forward primer (5'-AGAATTCAAGATGTGGCCCTGTGGCTCTGCTGGGC-3') and the reverse primer (5'-TTCTAGACTATGGCTGGAGCCTCCTTGGCACGAGCGCCCC-3') were used to amplify the coding region of ebaf with the 3' proofreading polymerase, Pfu (Stratagene, La Jolla, Calif.). The PCR products were separated in 1% agarose gel, and purified with a GeneClean kit (Biol01, LA Jolla, Calif.). The PCR products and the plasmids (pcDNA3 or HA-pcDNA3) were digested with EcoRI and XbaI (New England Lab, Beverly, Mass.). The fragments were annealed to a mammalian expression plasmid (pcDNA3 or HA-pcDNA3) with a Rapid Ligation Kit (Stratagene, Calif.). The sequence of the selected clone was validated by restriction enzyme digestion and by sequencing using Taq DyeDeoxy terminator cycle sequencing reactions in conjunction with an Applied Biosystems model 373 DNA Sequencer. The plasmid DNAs containing the correct cDNA sequence insertions were prepared using the Promega Wizard Miniprep Method (Promega, Madison, Wis.), and used for transfection.

Description of Disclosure:

[0073] C. Site-Directed Point Mutation of Human Ebaf

Description of Disclosure:

[0074] The N-glycosylation site of ebaf (amino acid residue 57) was point mutated to "D" using QuikChange.TM. 1-Day Site-Directed Mutagenesis kit (Stratagene, La Jolla, Calif.), following the manufacturer's protocol. The primers were DRTS-F: 5'-

GCGTCCGCGACGACGGCTCCGACCGCACCTCCCTCATCGACTCC-3'; DRTR-R: 5'-GGAGTCGATGAGGGAGGTGCGGTGCGAGCCGTCGTCGCGGACGC-3'. The sequences of all point-mutated clones were determined by Taq DyeDeoxy terminator cycle-sequencing reactions, in conjunction with an Applied Biosystems model 373 DNA Sequencer.

Description of Disclosure:

[0077] E. Affinity-Purification of Ebaf Protein

Description of Disclosure:

[0078] The inventor made two polyclonal antibodies to ebaf, A351 and A31, by immunizing a rabbit with either the C-terminus of ebaf (amino acid residues 351-367) or the N-terminus of ebaf (amino acid residues 31-43), respectively, and then affinity-purifying the resulting polyclonal antibodies. The inventor then purified ebaf proteins from culture media of HEK-293 cells stably transfected with ebaf. An affinity column was prepared by binding the A351 rabbit anti-ebaf peptide antibody to coupled Sepharose 4B.

Description of Disclosure:

[0079] The culture media of transfected cells were subjected to Western blotting, followed by staining blot with A351 antibody to verify production of ebaf. Confluent cultures of these cells were incubated overnight with serum-free DMEM medium in a CO.sub.2 incubator. The culture supernatant was collected and centrifuged at 1000.times.g to remove any cell or cell debris. For purification, urine and the cell-free medium were transferred to fresh tubes, mixed with 200 ml of ebaf-Sepharose 4B suspension, and incubated at room temperature for 1 h with gentle shaking. The Sepharose 4B was separated by centrifugation at 2000.times.g for 5 min, then washed 3 times in buffer A1 (0.05 M Tris HCl, 0.005 M EDTA, and 0.004 M A .epsilonpsilon.-aminocaproic acid), followed by 2 washes with buffer A2 (0.05 M Tris HCl, 0.005 M EDTA, 0.005 M ACA, 0.68 M NaCl), pH 7.4. The bound ebaf then was eluted by the addition of 1 ml of buffer B3 (0.06 M Tris HCl, 5 mM EDTA, 10% glycerol, 2% SDS), pH 5.5, at 37.degree. C. for 5 min. The mixture was centrifuged to remove the eluted ebaf. The gel matrix was washed once with 1 ml of elution buffer B3. Supernatant then was added to the first elution buffer. The buffer containing the eluted ebaf then was dialyzed against 3 changes of TE (10 mM Tris HCl and 1 mM EDTA), pH 7.5, at 4.degree. C., and was stored at 4.degree. C.

Description of Disclosure:

[0080] The amount of protein was measured by a commercially-available protein assay kit (Bio-Rad, Hercules, Calif.). The yield of ebaf was 40 ng for each ml of supernatant of confluent cultures. The two main secreted products of ebaf were separated by gel electrophoresis. The proteins then were eluted from the gel slices. Proteins were rendered visible in the gel by incubation with a buffer containing sodium acetate.

Description of Disclosure:

[0082] Proteins were extracted from tissues by directly placing the tissue in SDS lysis buffer. Ebaf was purified from sera and urine by affinity purification. In some cases, urine was concentrated 250-fold using a Centricon device with the molecular weight cutoff of 10 kD. Proteins were subjected to SDS-PAGE electrophoresis, and transferred to nitrocellulose membranes. Membranes were washed, then incubated with biotin-labeled goat anti-rabbit antiserum (1:2000 dilution) for 90 min at 25.degree. C. The membranes then were washed and incubated with the avidin-biotin-complex (ABC) reagent (1:300 dilution), for 30 min at 25.degree. C., and developed using the enhanced chemiluminescence system. The optical density of each band was determined by laser-scanning densitometry. Kruskal-Wallis and Mann-Whitney tests were used for statistical evaluation. Significance was established at the p<0.05 level.

Description of Disclosure:

[0085] A. Ebaf Proteins are Secreted.

Description of Disclosure:

[0086] To permit identification of the various forms of ebaf proteins which are synthesized and released by cells, ebaf cDNA was transfected into several cell lines. A mammalian expression vector containing the coding sequence of ebaf protein was used to transfect human embryonic kidney epithelial (HEK)-293 cells. The secretion of ebaf then was studied using two different assays.

Description of Disclosure:

[0087] In the first method, proteins were labeled in vivo by .sup.35S-methionine. Ebaf that was secreted into the culture medium was immunoprecipitated with an affinity-purified rabbit polyclonal A351 antibody against a C-terminus peptide of ebaf. The immunoprecipitate was subjected to SDS-PAGE (FIG. 1). In the second method, ebaf in the culture medium of transfected cells was affinity-purified, subjected to Western blotting, then probed using the A351 antibody (FIG. 1). In both assays, ebaf protein was detected as three protein bands of 42-, 34-, and 28-kD proteins in the culture medium of transfected cells. Smaller amounts of the 34- and 28-kD proteins were also found in the culture medium of nontransfected cells showing endogenous production of lower levels of ebaf by these cells. Similar results were obtained when other cell types, including NIH-3T3 cells and CHO cells, were transfected (data not shown).

Description of Disclosure:

[0088] To check the fate of the N-terminus pro-protein region of the ebaf proteins after processing by cells, the inventor generated a polyclonal antibody to an N-terminus peptide. This antibody (A31) was used to analyze the secretion of ebaf by transfected cells. Ebaf was affinity-purified from the culture medium of HEK-293 cells transfected with ebaf cDNA using two affinity columns: one made with the A351 antibody, and the other made with the A31 antibody. The eluates from these columns were subjected to Western blot analysis. One of the two identical blots was stained with the A351 antibody, and the other was stained with the A31 antibody (FIG. 2). Both antibodies detected the 42-kD protein in culture media of transfected cells. However, the 34- and 28-kD proteins only bound to the A351 affinity column; these were detected with the A351 antibody, but not with the A31 antibody. These findings suggest that the 42-kD protein is the precursor polypeptide, and that the 34- and 28-kD proteins are the C-terminus polypeptides processed from the precursor by proteolytic cleavage.

Description of Disclosure:

[0089] Proteins of the TGF-.beta. superfamily are cleaved by members of the pro-protein convertase (PC) family of endoproteases (Molloy et al., 1992; Dubois et al., 1995; and Cui et al., 1998). These endoproteases are Ca.sup.2+-dependent serine proteases with a consensus cleavage site of R-X-X-R (Bresnahan et al., 1990; Molloy et al., 1992; Dubois et al., 1995; and Cui et al., 1998). The inventor analyzed the ebaf sequence in order to identify the potential endoproteolytic processing sites of ebaf polypeptides, according to the consensus sequences required for convertase cleavage (Kothapalli et al., 1997). Two sequences, RGKR (amino acid residues 74-77) and RHGR (amino acid residues 132-135), were detected as potential cleavage sites for the processing of ebaf proteins. To ascertain whether these sequences are, indeed, the cleavage sites of ebaf in vivo, the inventor analyzed the effect on ebaf processing of the point mutations RGKR.fwdarw.GGKG (amino acid residues 74-77) and RHGR.fwdarw.GHGR (amino acid residues 132-135).

Description of Disclosure:

[0090] HEK-293 cells were transfected with the cDNA of ebaf mutants, and their culture medium was analyzed by Western blotting (FIG. 3). The mutation RGKR.fwdarw.GGKG (amino acid residues 74-77) inhibited processing of the 42-kD ebaf precursor to the 34-kD form. Contrastingly, the mutation RHGR.fwdarw.GHGR (amino acid residues 132-135) prevented the processing of the 28-kD, but not the 34-kD,



polypeptide form. These findings indicate that the proteolytic cleavage of the 28-kD polypeptide occurs independently of the proteolytic cleavage of the 34-kD polypeptide, suggesting that the cleavage at Arg-135 does not require either cleavage at Lys-77 or the formation of the 34-kD polypeptide. These results also rule out the possibility that these point mutations prevented the proteolytic cleavage at other potential cleavage sites.

Description of Disclosure:

[0091] B. Ebaf Proteins are Glycosylated.

Description of Disclosure:

[0092] The predicted size of the ebaf protein was smaller than the actual size that was determined for ebaf in immunoprecipitation and Western blot analyses. Moreover, the predicted sizes of the proteins derived from ebaf by cleavage at the RGKR and RHGR sites were also smaller than the actual sizes of these proteins when released into the culture media of transfected cells, suggesting that ebaf undergoes post-translational modification. The inventor detected one potential glycosylation site at amino acid 138 (N) in ebaf protein (Kothapalli et al., 1997). To assess the significance of this site in the glycosylation of ebaf, the inventor mutated "N" to "D", then transfected HEK-293 cells with the mutant cDNA. Cell lysates and the culture media of transfectants showed an approximately 3-kb reduction in the size of the 42-kD protein (FIG. 4A). Interestingly, the 34- and 28-kD proteins were not detected in the culture media of transfected cells, suggesting that proper processing of ebaf is dependent on glycosylation events.

Description of Disclosure:

[0093] To directly determine whether ebaf is glycosylated after release into the culture medium, ebaf was digested in vitro with Endo H, an enzyme that cleaves the glycosylated chain of proteins (FIG. 4B) at the high-mannose structures. Endo H digested ebaf to smaller-sized polypeptides. Despite prolonged incubation, digestion with Endo H was incomplete, and both the original-sized proteins and smaller proteins were detected. Therefore, the inventor sought to determine the effect of another enzyme, PNGase F, which is an amidase that cleaves between the innermost GlcNAc and asparagine residues of high-mannose and complex oligosaccharides from N-linked glycoproteins. PNGase F completely digested the 42-kD ebaf, as well as the 34- and 28-kD proteins, and resulted in production of proteins that were about 3-kb smaller in size (FIG. 4B).

Description of Disclosure:

[0094] C. Ebaf is Synthesized and Released by Bladder Carcinoma.

Description of Disclosure:

[0095] The inventor used bladder carcinoma as a paradigm to test the synthesis and release of ebaf by neoplastic epithelial cells. Tissue lysates of bladder carcinomas were subjected to Western blot analysis using A351 antibody. Ebaf protein was abundant in the bladder carcinoma, as compared with normal bladder mucosa (FIG. 5). The abundance and relative proportion of the 42-, 34-, and 28-kD proteins, however, markedly differed in different carcinomas. In almost all bladder carcinomas, the 42-kD protein was detected. However, the amount of 42- and 28-kD protein varied significantly, implying different aberrations in the processing of ebaf in these cancers. To better validate the relative abundance of ebaf in bladder carcinoma, the amount of ebaf in bladder carcinoma and in adjacent, noninvolved bladder mucosa was assessed by Western blotting. The results of this study showed the 42-kD protein to be more abundant in the carcinoma, as compared with noninvolved mucosa (FIG. 6A). However, the difference in the abundance of processed forms of ebaf in carcinoma, as compared with adjacent bladder mucosa, was less apparent.

Description of Disclosure:

[0096] To show that ebaf detected in Western blots of bladder cancers is present in

the carcinoma cells, rather than in cells in the stroma, tissue sections of the same cases were immunostained. Cryostat sections of the tumors were stained using the A351 anti-ebaf antibody. Ebaf was present both in the atypical epithelium adjacent to the tumors, and in the tumor cells themselves (FIG. 6B).

Description of Disclosure:

[0097] Since ebaf protein has to be secreted to release biologically-active proteins, the amount of ebaf protein in urine also was analyzed. Ebaf protein was affinity-purified from the urine of normal control subjects ranging in age from 7 to 78 years. The purified material then was assessed by Western blot analysis. Very little ebaf was detected in the urine of these subjects (FIG. 7A). Only in three patients were small quantities of 42-kD protein detected. The same analysis then was carried out on the urine of patients with hyperplasia and atypical hyperplasia of urothelium. Significantly higher amounts of ebaf were detected in atypical lesions, as compared with those that showed hyperplasia alone (FIG. 7B). In patients with transitional-cell carcinoma (TCC) of the bladder, significantly higher amounts of ebaf were detected in the urine (FIG. 7C). In most patients with low-grade TCC of the bladder, the amount of ebaf detected in the urine was lower than that detected in patients with high-grade lesions, including carcinoma in situ and high-grade papillary TCC of the bladder (FIG. 7C).

Description of Disclosure:

[0098] Since the ebaf detected in the urine of bladder cancer patients was mostly the 42-kD form, the amount of ebaf in the urine was directly analyzed in urine samples that had been concentrated using Centricon concentrating device (Amicon Co., Beverly, Mass.) with a 10,000-kD molecular weight cutoff. More of the secreted forms were detectable in the concentrated urine, as compared with those detected by affinity purification of the same amount of urine (FIG. 7D). These findings show a bias of the affinity column, in that it more preferentially allows the elution of the higher molecular-weight protein from the column.

Description of Disclosure:

[0099] Since ebaf is secreted into the urine of bladder cancer patients, the inventor considered the possibility that ebaf may directly or indirectly gain access to the peripheral circulation. To test this hypothesis, ebaf protein was affinity-purified from the sera of normal male control subjects. Since ebaf is associated with the menstrual cycle, and its expression is enhanced around the time of menses, sera were also obtained from women during the menstrual cycle and around the time of menses. Ebaf was affinity-purified from these sera, and the purified material then was assessed by Western blot analysis. Very little ebaf was detected in the sera of these normal subjects (FIG. 8A). In contrast, significantly higher amounts of ebaf were detected in the sera of patients with bladder carcinomas (FIG. 8A).

Description of Disclosure:

[0100] To determine whether the amount of ebaf detected in the urine correlated with the amount of ebaf detected in the sera of bladder cancer patients, ebaf was purified from the urine and sera of the same subjects, then subjected to Western blotting. Ebaf was detected both in the urine and sera of these cancer patients. Moreover, more ebaf was found in the sera of patients in whom more ebaf was detected in the urine samples (FIG. 8B). Thus, the amounts appeared to correlate.

Description of Disclosure:

[0101] Ebaf protein is overexpressed in certain human carcinomas, but the significance of this overexpression is poorly understood (Tabibzadeh et al., 1997). To better understand the function of this protein, there is a need to identify its processed and biologically-active forms. TGF- $\beta$  superfamily members are synthesized as large precursors, and their signal peptide is rapidly removed within the cell to produce a large precursor protein. The best-studied example of processing has been shown for TGF- $\beta$ 1, which is expressed as an inactive

precursor of 55 kD. TGF- $\beta$ .1 precursor is cleaved to produce the pro-TGF- $\beta$ .1 of 44 kD, and a final polypeptide of 12.5 kD that becomes biologically active in a homodimer form (Dubois et al., 1995).

Description of Disclosure:

[0102] Herein, the inventor has shown that ebaf is processed to form two cleavage products from a single precursor protein. Transfection with ebaf of HEK-293 and Chinese hamster ovary (CHO) cells showed secretion of three polypeptides of 42, 34, and 28 kD. Characterization of the secreted proteins, both with immunoprecipitation and Western blotting, showed proteins of similar size in the culture media of transfected cells. Smaller quantities of the 34-kD protein were found in the HEK-293 cells, suggesting that ebaf is endogenously synthesized in these cells. In order to identify whether ebaf is endoproteolytically processed, the inventor mutated two potential cleavage sites. The point mutations at the pro-protein convertase (PC) consensus sequences, RGKR (amino acid residues 74-77) and RHGR (amino acid residues 132-135), prevented the formation of the 34-kD and 28-kD ebaf polypeptides, respectively. In view of these data, the inventor suggests that ebaf is synthesized as a 42-kD protein which is proteolytically cleaved at Arg 77 to release the 34-kD polypeptide. The 28-kD ebaf polypeptide is produced by cleavage of the ebaf polypeptide at Arg 132.

Description of Disclosure:

[0103] The sizes of the proteins released into the culture media of transfected cells were larger than their predicted sizes, suggesting that ebaf undergoes post-translational modifications after synthesis. To show such modification, the inventor mutated the single potential glycosylation site of ebaf. The point mutation, DRTS (amino acid residue 158).fwdarw.NRTS, led to a loss of approximately 3 kD in the size of the protein, indicating that ebaf is glycosylated at Asp 158. Interestingly, the 34- and 28-kD forms were not detected. Since post-translational modifications, including endoproteolytic processing, take place within the Golgi complex after N-glycosylation (Molloy et al., 1999), the findings imply that a lack of glycosylation events impairs the endoproteolytic processing of ebaf protein. Since point mutation of ebaf did not show whether the 34- and 28-kD proteins are glycosylated, ebaf proteins were digested in vitro with Endo H and PNGase F. Endo H only partially digested ebaf proteins, whereas PNGase F led to complete digestion of ebaf proteins and formation of proteins that were all approximately 3 kD smaller than the undigested forms. These findings confirm that all secreted forms of ebaf proteins are glycosylated.

Description of Disclosure:

[0104] The N-terminus protein released from proteolytic processing of TGF- $\beta$ .1 plays a role in the biologic fate of TGF- $\beta$ .1. TGF- $\beta$ .1 is released as a latent complex composed of mature TGF- $\beta$ .1, the N-terminal remnant of the TGF- $\beta$ .1 precursor (TGF- $\beta$ .1-latency associated peptide), and the latent TGF- $\beta$ .1 binding protein (LTBP) (Wakefield et al., 1988; and Miyazono et al., 1991). To address the fate of the N-terminus pro-protein region of the ebaf proteins, the inventor assessed potential presence of the N-terminus protein(s) by Western blotting using the A31 antibody. This analysis showed that the A31 antibody detected the presence of the 42-kD ebaf precursor. However, N-terminus proteins were not detected in the culture medium, thereby suggesting either that they are not secreted or that they are rapidly removed from the culture medium.

Description of Disclosure:

[0105] The inventor used transitional-cell carcinoma (TCC) of the bladder as a paradigm to analyze the synthesis and secretion of ebaf protein in vivo. Ebaf precursor and its endoproteolytically-processed forms were detected in the bladder carcinoma. The size of the precursor was slightly larger than that detected in the transfected cells, suggesting a more complex post-translational modification in tissues in vivo. Moreover, the extent to which the precursor and processed forms were detected varied among different tumors. In some tumors, the precursor was more

abundant; in other tumors, only the 34- and the 28-kD forms were found in excess. This suggests that the proteolytic processing and/or release of ebaf is different or may be impaired in different bladder cancers.

Description of Disclosure:

[0107] Recent studies have revealed genetic alterations in the bladder carcinomas. One of the most common genetic alterations is allelic losses on chromosomes 4, 8, 9, 11, and 17 (Czerniak et al., 2000). The majority of statistically-significant allelic losses (70%) occurred early in low-grade intraurothelial dysplasia, and some of them involved adjacent areas of morphologically-normal mucosa preceding the development of microscopically-recognizable precursor lesions. For this reason, the inventor assessed the amount of ebaf in bladder carcinomas and in the adjacent, grossly-unremarkable tissues. This analysis showed the 42-kD ebaf protein to be more abundant in the bladder carcinomas, while the processed forms of ebaf were more abundant in adjacent tissues. These findings show that progression to carcinoma is associated with either the impairment of synthesis or the release of the processed forms of the ebaf protein.

Description of Disclosure:

[0108] TGF- $\beta$  superfamily members are secreted. Therefore, in order to detect the secreted forms of ebaf, the inventor first analyzed urine obtained from normal subjects. There were very small quantities of ebaf in these urine samples. In contrast, the urine of cancer patients contained abundant amounts of ebaf, indicating that ebaf protein is rapidly secreted by the cancer cells into the urine. Although the ebaf protein detected by affinity purification was mostly the 42-kD protein, the processed forms of the proteins were also detected. These processed forms were more frequently observed when ebaf was detected by Western blotting of concentrated urine, rather than by Western blotting of ebaf that had been affinity purified from urine.

Description of Disclosure:

[0109] The overexpression of ebaf in TCC of the bladder is presumably the consequence of genetic alterations, and is associated with other genetic alterations in bladder carcinomas. Multiple genetic alterations have been described in bladder carcinomas (Orntoft and Wolff, 1998). The loss of heterozygosity has shown a general chromosomal instability in TCC of the bladder, with loss of parts of chromosome 9 in papillomas, and loss of parts of chromosomes 11, 13, 3, 4, 8, 17, and 18 during further development of the tumor. Activation of oncogenes is exemplified by mutations found in the ras gene family, and by overexpression of the c-erbB-2 gene in a smaller number of tumors. The loss of one p53 allele is common in TCC of the bladder, and the expression of p16 and p15, the cell cycle factors, is lost in these tumors. These alterations correlate well with survival, disease progression, invasion, and recurrence of TCC of the bladder. The downregulation of the ABO gene, followed by loss of ABO blood group structures and accumulation of the Lewis cell adhesion molecules, has been reported in high-grade tumors (Orntoft and Wolff, 1998).

Description of Disclosure:

[0111] Recently, other biomarkers that are correlated with grade and stage of TCC of the bladder have been identified by functional proteome analysis (Orntoft and Wolff, 1998). Biomarkers currently used for screening and detection of bladder cancer are the nuclear matrix protein, NMP-22; human complement factor H related protein (BTA stat); FDP; chemiluminescent hemoglobin; hemoglobin dipstick; and telomerase assay. Among these, telomerase assay seems to offer greater sensitivity and specificity (Landman et al., 1998; and Ramakumar et al., 1999). Quantification of ebaf also may be a useful biomarker for screening for TCC of the bladder, and potentially may be used for determining and predicting the survival, disease progression, invasion, and recurrence of the disease by analysis of urine, serum, other bodily fluids, and cells or tissues obtained from the urinary tract.

Description of Disclosure:

[0112] The spectrum of changes detected in bladder have been recently re-classified by the World Health Organization. According to the new classification, flat urothelial lesions include hyperplasia, reactive atypia/atypia of unknown significance, dysplasia, and carcinoma in situ. Papillary urothelial lesions include papillomas, papillary neoplasms of low malignant potential, and papillary carcinomas (Helpap et al., 2000). Separation of the bladder tumors used in this study, in accordance with this classification, revealed that ebaf was detected at a low level in the urine of patients with hyperplasia, but that significantly higher levels were found in the urine of patients with flat carcinoma in situ. In the majority of patients who had low-grade papillary transitional-cell carcinoma, amounts of ebaf found in the urine were lower than the amounts of ebaf found in the urine of patients with high-grade carcinomas. These findings show that the overexpression of ebaf correlates with the degree of morphologic differentiation of transitional-cell carcinomas, with those having a poor prognosis showing the potential to secrete more ebaf into the urine.

Description of Disclosure:

[0113] 1. Baniel, J., Bladder cancer in women. Int. Urogynecol. J. Pelvic Floor Dysfunct., 10(6):399-404, 1999. [0114] 2. Beers and Berkow, eds., The Merck Manual of Diagnosis and Therapy, 17.sup.th ed. (Whitehouse Station, N.J.: Merck Research Laboratories, 1999) 1814, 1917. [0115] 3. Bresnahan et al., Human fur gene encodes a yeast KEX2-like endoprotease that cleaves pro-beta-NGF in vivo. J. Cell Biol., 111:2851-59, 1990. [0116] 4. Cui et al., BMP-4 is proteolytically activated by furin and/or PC6 during vertebrate embryonic development. EMBO J., 17(16):4735-43, 1998. [0117] 5. Czerniak et al., Genetic modeling of human urinary bladder carcinogenesis. Genes Chromosomes Cancer, 27(4):392-402, 2000. [0118] 6. Dubois et al., Processing of transforming growth factor beta 1 precursor by human furin convertase. J. Biol. Chem., 270(18):10618-24, 1995. [0119] 7. Eder et al., Transforming growth factors-beta 1 and beta 2 in serum and urine from patients with bladder carcinoma. J. Urol., 156(3):953-57, 961, 1996. [0120] 8. Eder et al., Expression of transforming growth factors beta-1, beta 2 and beta 3 in human bladder carcinomas. Br. J. Cancer, 75(12):1753-60, 1997. [0121] 9. Farrow, G. M., Pathology of carcinoma in situ of the urinary bladder and related lesions. J. Cell. Biochem., Suppl; 161:39-43, 1992. [0122] 10. Helpap and Kollermann, Revisions in the WHO histological classification of urothelial bladder tumors and flat urothelial lesions. 21(3):211-17, 2000. [0123] 11. Kosaki et al., Characterization and mutation analysis of human LEFTY A and LEFTY B, homologues of murine genes implicated in left-right axis development, Am. J. Hum. Genet, 64(3):712-21, March 1999. [0124] 12. Kothapalli et al., Detection of ebaf, a novel human gene of the TGF-beta. superfamily; association of gene expression with endometrial bleeding J. Clin. Invest., 99:2342-50, 1997. [0125] 13. Lamb et al., Neural induction by the secreted polypeptide noggin. Science, 262(5134):713-18, 1993. [0126] 14. Landman et al., Sensitivity and specificity of NMP-22, telomerase, and BTA in the detection of human bladder cancer. Urology, 52(3):398-402, 1998. [0127] 15. Madrid Garcia et al., Transitional cell bladder carcinoma in patients younger than 40 years of age. Arch. Esp. Urol., 51(10):991-4, 1998. [0128] 16. Meno et al., Left-right asymmetric expression of the TGF beta-family member lefty in mouse embryos. Nature, 381(6578):151-5, 1996. [0129] 18. Meno et al., Two closely-related left-right asymmetrically expressed genes, lefty-1 and lefty-2: their distinct expression domains, chromosomal linkage and direct neuralizing activity in Xenopus embryos. Genes Cells, 2(8):513-24, 1997. [0130] 19. Meno et al., Lefty-1 is required for left-right determination as a regulator of lefty-2 and nodal. Cell, 94(3):287-97, 1998. [0131] 20. Metts et al., Bladder cancer: a review of diagnosis and management. J. Natl. Med. Assoc., 92(6):285-94, 2000. [0132] 21. Miyamoto et al., Expression of transforming growth factor-beta 1 in human bladder cancer. Cancer, 75(10):2565-70, 1995. [0133] 22. Miyazono et al., A role of the latent TGF-beta 1-binding protein in the assembly and secretion of TGF-beta 1. EMBO J., 10(5):1091-101, 1991. [0134] 23. Molloy et al., Human furin is a calcium-dependent serine endoprotease that recognizes the sequence Arg-X-X-Arg and efficiently cleaves

anthrax toxin protective antigen. J. Biol. Chem., 267(23):16396-402, 1992. [0135] 24. Molloy et al., Bi-cycling the furin pathway: from TGN localization to pathogen activation and embryogenesis. Trends Cell Biol., 9(1):28-35, 1999. [0136] 25. Orntoft and Wolff, Molecular alterations in bladder cancer. Urol. Res., 26(4):223-33, 1998. [0137] 26. Ramakumar et al., Comparison of screening methods in the detection of bladder cancer. J. Urol., 161(2):388-94, 1999. [0138] 27. Seth et al., Vary CP Coordinate expression of novel genes during osteoblast differentiation. J. Bone Miner. Res., 15(9):1683-96, 2000. [0139] 28. Sha et al., Transforming growth factor beta 1: importance of glycosylation and acidic proteases for processing and secretion. Mol. Endocrinol, 3:1090-98, 1989. [0140] 29. Soloway, M. S., Managing superficial bladder cancer: an overview. Urology, 40(6 Suppl.):5-10, 1992. [0141] 30. Spruck et al., Two molecular pathways to transitional cell carcinoma of the bladder. Cancer Res., 54(3):784-88, 1994. [0142] 32. Tabibzadeh et al., Distinct tumor specific expression of TGFB4 (ebaf), a novel human gene of the TGF-beta superfamily. Front. Biosci., 2:a18-25, 1997. [0143] 33. Van de Loo et al., Biosynthesis, distinct post-translational modifications, and functional characterization of lymphoma proprotein convertase. J. Biol. Chem., 272(43):27116-23, 1997. [0144] 34. Wakefield et al., Latent transforming growth factor-beta from human platelets. A high molecular weight complex containing precursor sequences. J. Biol. Chem., 263(16):7646-54, 1988.

## CLAIMS:

1. A method for determining whether a subject has a pre-neoplastic or neoplastic lesion in transitional epithelial cells, comprising assaying a diagnostic sample of the subject for ebaf expression, wherein ebaf expression elevated above normal is diagnostic of a pre-neoplastic or neoplastic lesion in transitional epithelial cells.
7. The method of claim 1, wherein the diagnostic sample is assayed using an agent reactive with ebaf.
11. The method of claim 1, wherein the diagnostic sample is assayed using at least one nucleic acid probe which hybridizes to nucleic acid encoding ebaf.
14. A method for assessing the efficacy of therapy to treat a pre-neoplastic or neoplastic lesion in transitional epithelial cells in a subject who has undergone or is undergoing treatment for a pre-neoplastic or neoplastic lesion in transitional epithelial cells, comprising assaying a diagnostic sample of the subject for ebaf expression, wherein normal ebaf expression is indicative of successful therapy to treat a pre-neoplastic or neoplastic lesion in transitional epithelial cells, and ebaf expression elevated above normal is indicative of a need to continue therapy to treat a pre-neoplastic or neoplastic lesion in transitional epithelial cells.
17. The method of claim 14, wherein the diagnostic sample is assayed using an agent reactive with ebaf.
21. The method of claim 14, wherein the diagnostic sample is assayed using at least one nucleic acid probe which hybridizes to nucleic acid encoding ebaf.
24. A method for assessing the prognosis of a subject who has a pre-neoplastic or neoplastic lesion in transitional epithelial cells, comprising assaying a diagnostic sample of the subject for ebaf expression, wherein the subject's prognosis improves with a decrease in ebaf expression in the diagnostic sample of the subject.

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## WEST Search History





DATE: Friday, June 23, 2006

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	<i>DB=USPT; PLUR=YES; OP=OR</i>		
<input type="checkbox"/>	L1	5916751.pn.	1
<input type="checkbox"/>	L2	lyscysalaser	0
<input type="checkbox"/>	L3	cys-lys-cys	1
	<i>DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD; PLUR=YES; OP=OR</i>		
<input type="checkbox"/>	L4	cys-lys-cys	1
<input type="checkbox"/>	L5	ckc	573
<input type="checkbox"/>	L6	L5 and cystine	11
<input type="checkbox"/>	L7	anticysteine or anti-cysteine or (antibodies near cysteine)	2441
<input type="checkbox"/>	L8	anticysteine or anti-cysteine	3
<input type="checkbox"/>	L9	monoclonal near cysteine	0
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<input type="checkbox"/>	L11	cys-ala	47
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<input type="checkbox"/>	L13	antiproline or anti-proline	0
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<input type="checkbox"/>	L16	glycine near antibodies	52
<input type="checkbox"/>	L17	L16 not l5	52
<input type="checkbox"/>	L18	l16 not l15	51

END OF SEARCH HISTORY

1: Philos Trans R Soc Lond B Biol Sci. 1990 Mar 12;327(1239):145-54.

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## **Transforming growth factor-beta: multifunctional regulator of differentiation and development.**

**Roberts AB, Flanders KC, Heine UI, Jakowlew S, Kondaiah P, Kim SJ, Sporn MB.**

Laboratory of Chemoprevention, National Cancer Institute, Bethesda, Maryland 20892.

Transforming growth factors-beta (TGF-beta) are 25 kilodalton (kDa) homodimeric peptides with multifunctional actions controlling the growth, differentiation and function of a broad range of target cells of both epithelial and mesenchymal derivation. They are expressed early in embryogenesis and their tissue-specific and developmentally dependent expression is strongly suggestive of an essential role in particular morphogenetic and histogenetic events. Five distinct TGF-beta s have been characterized so far, with 65-80% homology to each other. By using both molecular biological and immunohistochemical techniques, we are currently attempting to define specific sites of expression of the different TGF-beta s and to determine whether TGF-beta s 1-5 might have unique functions in development and in the mature organism. Comparative study of the promoter regions for the different TGF-beta s and for any particular TGF-beta in different species is also underway. Mechanistically, TGF-beta s act to control gene expression of their target cells, many of their actions converging on a complex, multifaceted scheme of control of matrix proteins and their interactions with cells; these effects on matrix are thought to mediate many of the effects of TGF-beta on development.

Publication Types:

- Review

PMID: 1969655 [PubMed - indexed for MEDLINE]

have

DGAL  
GALP

W09605224

5616561

Barcellos-Holb

1997

Wintrow  
S. Z. Gendelman



tr	Q53H67	Left-right determination, factor B preproprotein variant	366
	Q53H67_HUMAN	(Fragment)	AA
		[LEFTY1] [Homo sapiens (Human)]	align

Score = 43.5 bits (95), Expect = 8e-04

Identities = 13/13 (100%), Positives = 13/13 (100%)

Query: 1 CASDGALVPRRLQ 13

CASDGALVPRRLQ

Sbjct: 353 CASDGALVPRRLQ 365

**NUCLEOTIDE SEQUENCE.**

**TISSUE**=Colon;

DOI=10.1016/0378-1119(94)90802-8;

PubMed=8125298 [NCBI, ExPASy, EBI, Israel, Japan]

Maruyama K., Sugano S.;

"Oligo-capping : a simple method to replace the cap structure of eucaryotic mRNAs with oligoribonucleotides.";

Gene 138:171-174(1994).

[2]

**NUCLEOTIDE SEQUENCE.**

**TISSUE**=Colon;

DOI=10.1016/S0378-1119(97)00411-3;

PubMed=9373149 [NCBI, ExPASy, EBI, Israel, Japan]

Suzuki Y., Yoshitomo K., Maruyama K., Suyama A., Sugano S.;

"Construction and characterization of a full length-enriched and a 5'-end-enriched cDNA library.";

Gene 200:149-156(1997).

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# UniProtKB/TrEMBL entry Q53H67



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*Note: most headings are clickable, even if they don't appear as links. They link to the user manual or other documents.*

## Entry information

Entry name	<b>Q53H67_HUMAN</b>
Primary accession number	<b>Q53H67</b>
Secondary accession numbers	None
Integrated into TrEMBL on	May 24, 2005
Sequence was last modified on	May 24, 2005 (Sequence version 1)
Annotations were last modified on	May 30, 2006 (Entry version 8)
<b>Name and origin of the protein</b>	
Protein name	<b>Left-right determination, factor B preproprotein varia [Fragment]</b>
Synonyms	None
Gene name	<b>Name: LEFTY1</b>
From	Homo sapiens (Human) [TaxID: 9606]
Taxonomy	Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Euarchontoglires; Primates; Haplorrhini; Catarrhini; Hominidae; Homo.

## References

### [1] NUCLEOTIDE SEQUENCE.

**TISSUE**=Colon;

DOI=10.1016/0378-1119(94)90802-8; PubMed=8125298 [NCBI, ExPASy, EBI, Israel, Jap  
Maruyama K., Sugano S.;

"Oligo-capping : a simple method to replace the cap structure of eucaryotic mRNAs with  
oligoribonucleotides.";

Gene 138:171-174(1994).

### [2] NUCLEOTIDE SEQUENCE.

**TISSUE**=Colon;

DOI=10.1016/S0378-1119(97)00411-3; PubMed=9373149 [NCBI, ExPASy, EBI, Israel, Jap  
Suzuki Y., Yoshitomo K., Maruyama K., Suyama A., Sugano S.;

"Construction and characterization of a full length-enriched and a 5'-end-enriched cDNA library.";

Gene 200:149-156(1997).

### [3] NUCLEOTIDE SEQUENCE.

**TISSUE**=Colon;

Suzuki Y., Sugano S., Totoki Y., Toyoda A., Takeda T., Sakaki Y., Tanaka A., Yokoyama

Submitted (APR-2005) to the EMBL/GenBank/DDBJ databases.

### Comments

- **SIMILARITY:** Belongs to the TGF-beta family.

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### Cross-references

#### Sequence databases

EMBL AK222714; BAD96434.1; -; mRNA.[EMBL / GenBank / DDBJ] [CoDingSequenc

#### 3D structure databases

ModBase Q53H67.

#### 2D gel databases

SWISS-2DPAGE Get region on 2D PAGE.

#### Organism-specific gene databases

HOVERGEN [Family / Alignment / Tree]

### Ontologies

GO GO:0008083; Molecular function: growth factor activity (*inferred from electronic annotation*).

GO GO:0005160; Molecular function: transforming growth factor beta receptor bind (*inferred from electronic annotation*).

GO GO:0016049; Biological process: cell growth (*inferred from electronic annotation*)

QuickGo view.

### Family and domain databases

InterPro IPR001839; TGFb.

InterPro IPR003942; TGFb4.

InterPro IPR001111; TGFb\_N.

Graphical view of domain structure.

Pfam PF00019; TGF\_beta; 1.

Pfam PF00688; TGFb\_propeptide; 1.

Pfam graphical view of domain structure.

PRINTS PR01427; TGFBETA4.

ProDom PD000357; TGFb; 1.

[Domain structure / List of seq. sharing at least 1 domain]

SMART SM00204; TGFB; 1.

SMART graphical view of domain structure.

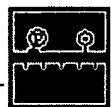
PROSITE PS00250; TGF\_BETA\_1; 1.

### Genome annotation databases

Ensembl ENSG00000143787; Homo sapiens. [Contig view]

**Other**

UniRef View cluster of proteins with at least 50% / 90% / 100% identity.

**Keywords****Growth factor.****Features**

Feature table viewer

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**Sequence information**

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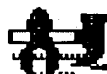
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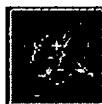
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ExpASY/SIB  
or at NCBI (USA)



Sequence analysis tools: ProtParam,  
ProtScale, Compute pI/Mw, PeptideMass,  
PeptideCutter, Dotlet (Java)



ScanProsite, MotifScan



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SWISS-MODEL



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## EBI Dbfetch

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DE   variant, clone: COL03075.
XX
KW   FLI_CDNA; oligo capping.
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OC   Homo.
XX
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RP   1-1644
RA   Suzuki Y., Sugano S., Totoki Y., Toyoda A., Takeda T., Sakaki Y.,
RA   Tanaka A., Yokoyama S.;
RT   ;
RL   Submitted (22-APR-2005) to the EMBL/GenBank/DDBJ databases.
RL   Akiko Tanaka, RIKEN Yokohama Institute, Protein Research Group; 1-7-22
RL   Suehiro, Tsurumi, Yokohama, Kanagawa, 230-0045, Japan
RL   (E-mail:aktanaka@riken.jp, URL:http://protein.gsc.riken.jp/,
RL   Tel:81-45-503-9452, Fax:81-45-503-9450)
XX
RN   [2]
RX   DOI; 10.1016/0378-1119(94)90802-8
RX   PUBMED; 8125298.
RA   Maruyama K., Sugano S.;
RT   "Oligo-capping : a simple method to replace the cap structure of eucaryotic
RT   mRNAs with oligoribonucleotides.";
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RT   "Construction and characterization of a full length-enriched and a
RT   5'-end-enriched cDNA library.";
RL   Gene 200(1-2):149-156(1997).
XX
CC   This work was supported in part by the National Project on Protein
CC   Structural and Functional Analysis, Ministry of Education,
CC   Culture, Sports, Science and Technology of Japan.
CC   Sumio Sugano, Yutaka Suzuki
CC   Laboratory of Functional Genomics Department of Medical Genome
CC   Sciences Graduate School of Frontier Sciences The University of
CC   Tokyo, 4-6-1 Shirokanedai, Minato-ku, Tokyo 108-8639 Japan
CC   email: ssugano@k.u-tokyo.ac.jp
CC   URL: http://www.k.u-tokyo.ac.jp/index.html.en
  
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24. 6479643. 02 Feb 00; 12 Nov 02. Single chain analogs of the TGF- $\beta$  superfamily (morphons). Keck; Peter C., et al. 530/399; 530/350. C12N015/12 C07K014/51 .

25. 6040431. 07 Jun 95; 21 Mar 00. Single chain analogs of the TGF- $\beta$  superfamily (morphons). Keck; Peter C., et al. 530/399; 530/350. C12N015/12 C07K014/51 .

☐ 26. 6030617. 06 Oct 97; 29 Feb 00. Use of growth differentiation factor-9 (GDF-9) to inhibit oocyte maturation. Lee; Se-Jin. 424/158.1; 424/130.1 424/133.1 424/139.1 424/141.1 424/142.1 424/145.1. A61K039/395 .

☐ 27. 5821056. 23 Oct 95; 13 Oct 98. Growth differentiation factor-9. Lee; Se-Jin. 435/6; 435/252.3 435/320.1 435/325 435/7.1 530/350 530/397 530/399 536/23.5 536/23.51 536/24.31. C07K014/475 C12N001/21 C12N005/10 C12N015/12 .

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